Examining the association between future pregnancy intentions, contraceptive use and repeat pregnancies among women living with HIV in Cape Town, South Africa

Lilian Tuhumwire Mubangizi

MBNLIL001

submitted to the University of Cape Town
in partial fulfilment of the requirements for the degree

Master of Public Health in Epidemiology

School of Public Health & Family Medicine, Faculty of Health Sciences
UNIVERSITY OF CAPE TOWN

Date of Submission: 10 February 2020

Supervisor(s): Dr Kirsty Brittain

Co-supervisor: Prof. Landon Myer

DECLARATION

I, *Lilian Tuhumwire Mubangizi*, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Signature: Signed by candidate

Date: 10/02/2020

Acknowledgements

Firstly, I would like to express my sincere gratitude to my supervisor Dr Kirsty Brittain for the constant guidance, feedback and support throughout the process of writing this thesis. Your guidance has pushed me to become more analytical and allowed me to become a better writer.

Secondly, I would like to thank my co-supervisor Prof. Landon Myer for allowing me to work on this project and for your guidance in the conception of the research question.

Abstract

Background: Given the rapid expansion of antiretroviral therapy (ART) services in South Africa, there is growing recognition of the importance of fertility intentions, contraceptive use and childbearing among women living with HIV (WLHIV). With the integration of family planning services in the prevention of mother-to-child transmission of HIV (PMTCT) services, understanding fertility intentions and contraceptive use is crucial in evaluating such programs. We investigated the relationship between future fertility intentions, contraceptive use and repeat pregnancies among WLHIV in Cape Town, South Africa.

Methodology: We analyzed data from the MCH-ART study conducted at the Gugulethu Midwife Obstetric Unit (MOU) in Cape Town, South Africa, which followed women initiating ART during pregnancy through 36-60 months postpartum. Self-report data were collected using standardized questionnaires at repeated study visits. Data on repeat pregnancies were abstracted from the Western Cape Provincial Data Centre. Associations between maternal characteristics and repeat pregnancies were examined using Cox proportional hazards models.

Results: Overall, 109 incident repeat pregnancies were recorded among the 471 women included in this analysis. The median time at risk per individual was 4.27 years. The rate of repeat pregnancies was 5.72 per 100 person-years (PY). This rate was significantly lower among women aged 35-45 years (2.11/100PY) compared to women aged 18-24 years [7.56/100 PY; adjusted hazard ratio (aHR), 0.26: 95% confidence interval [CI], 0.09, 0.81). A total of 333 women contributed data on future fertility intentions and contraceptive use at 12 months postpartum, with 9% reporting that they wanted another child in the future, and 82% reporting current contraceptive use; 16% (n=54) reported not wanting another child but no contraceptive use. The rate of repeat pregnancies was 3 folds higher among women who reported wanting a child in the future (12.59/100 PY) compared to women who did not want

a child in the future (4.31/100 PY; aHR, 3.46: 95% CI, 1.83, 6.50). Contraceptive use at 12 months postpartum was not associated with repeat pregnancies. Women who did not want a child and used contraceptives had a 45% decreased hazard of repeat pregnancies compared to women who did not want a child and did not use contraceptives (aHR 0.55: 95% CI [0.32, 0.94].

Conclusion: Among women initiating ART during pregnancy, a repeat pregnancy incidence rate of 5.72/100 PY was observed through 36-60 months postpartum, with the incidence lower among older women. At 12 months postpartum, a notable proportion of women reported not wanting another child but no contraceptive use. Wanting a child in the future was associated with a higher rate of repeat pregnancy, but contraceptive use at 12 months postpartum was not associated with repeat pregnancies. These results highlight the importance of understanding factors associated with the dissonance between fertility intentions and contraceptive use and childbearing to ensure delivery of quality integrated reproductive health services in the PMTCT framework.

Table of Contents

DECLARATION 2
ACKNOWLEDGEMENTS 3

ABSTRACT **4**

SECTION A: RESEARCH PROTOCOL **8**

BACKGROUND 9
RATIONALE 12
METHODS 13
Study Design *13*
Study setting *13*
Data collection *14*
DATA MANAGEMENT AND ANALYSIS 18
Data Management *18*
Data Analysis *18*
ETHICAL CONSIDERATIONS 19
Informed consent *19*
Privacy and confidentiality *19*
Risks and benefits *19*
DISSEMINATION OF RESULTS 20
STUDY TIMELINE 21

SECTION B: LITERATURE REVIEW **25**

OBJECTIVE OF LITERATURE REVIEW 26
METHODOLOGY 26
TRENDS AND DETERMINANTS OF FERTILITY INTENTIONS 27
Trends *27*
Determinants of fertility intentions *28*
Synthesis *32*
TRENDS AND DETERMINANTS OF CONTRACEPTIVE USE 35
Trends *35*
Determinants *35*
Synthesis *38*
TRENDS OF PREGNANCIES AND REPEAT PREGNANCIES 39
FACTORS ASSOCIATED WITH PREGNANCY OCCURRENCE 40
CONCLUSION: AREAS FOR FURTHER RESEARCH 41

SECTION C: MANUSCRIPT **54**

INTRODUCTION 55
METHODS 56
Study Setting and Population *56*
Inclusion and Exclusion Criteria *56*
Data Collection *56*
Data Analysis *57*
RESULTS 59
Sociodemographic characteristics of the study subjects *59*
Reproductive, obstetric, and fertility intentions of study subjects *59*
Incidence rate of repeat pregnancy *60*
DISCUSSION 64
Conclusion *66*

SECTION D: APPENDIX **69**

A. FUTURE FERTILITY INTENTIONS AND CONTRACEPTIVE USE QUESTIONNAIRE 70
B. ETHICAL APPROVAL 71
C. MCH-ART ICAP IRB APPROVAL 73

D. MCH-ART UCT HREC Approval....75
E. MCH-ART Informed consent forms....77
F. JIAS author guidelines....83

SECTION A: RESEARCH PROTOCOL

Background

Prevention of mother-to-child transmission (PMTCT) of HIV continues to be a public health priority following the success of antiretroviral therapy (ART) [1]. Ongoing research and programmatic experience have presented cost-effective strategies to reduce the incidence of paediatric cases in resource-limited settings [1]. In Sub Saharan Africa, the emphasis is on the scaling-up of cost-effective PMTCT interventions to prevent paediatric infections. PMTCT interventions in South Africa have been successful covering an estimated 95% of women living with HIV (WLHIV) [1,4].

The World Health Organization (WHO) promotes a comprehensive PMTCT approach which includes prevention of HIV among women of childbearing age, preventing unintended pregnancies, preventing mother-to-child transmission (MTCT), and providing treatment, care, and support to women and their families [1]. To date, the focus has mainly been on providing antiretroviral drugs and preventing HIV. There has been less focus on understanding the reproductive intentions and contraceptive use among women on ART, potentially limiting the ability to prevent unintended pregnancies and to provide care and support to WLHIV [1].

Women, including WLHIV, have the right to bear the number of children they desire with spacing that suits them. Like uninfected women, WLHIV desire additional pregnancies and have fertility intentions that change over time. Evidence suggests ART use is associated with increased pregnancy incidence [2], although future fertility intentions may increase independent of ART use [3]. Research from South Africa has suggested that over one-third of women on ART become pregnant [2], and approximately 40 - 50% of women on ART in Ethiopia desire to have children [4, 5]. In a study conducted in Kenya between 2003 to 2009, the incidence of repeat pregnancies among WLHIV was 17.6 % [6]. Research from South Africa and Ethiopia suggests that low levels of education, low economic status and younger

maternal age are associated with an increased incidence of repeat pregnancies [6, 7]. Previous contraceptive use is associated with decreased odds of repeat pregnancies [4, 6].

Incidence of pregnancy among WHLIV has important implications for their health, as well as their infant's and partner's health [8]. Pregnancy without precaution may lead to transmission of HIV to their partner and infant [9]. Fertility intentions may have long-term consequences on maternal health behaviours such as health-seeking and substance abuse; and health trajectories such as depression [8]. Provision of appropriate family planning services is important to guide WHLIV through safe conception. In South Africa, women receive PMTCT services within the antenatal clinic during pregnancy but are referred to general adult ART services immediately postpartum. Provision of family planning services within PMTCT programs and general ART services is important in South Africa to prevent the negative implications of unplanned pregnancies. Integration of family planning services into PMTCT and adult ART services is critical in supporting women's fertility choices and encouraging contraceptive use.

Evidence suggests that even in developed countries with advanced HIV care, only 25% of WLHIV discuss future fertility intentions with their health care providers [10]. Lack of reproductive health services may lead to an increased incidence of unintended pregnancies, the transmission of HIV among serodiscordant couples and increased incidence of mother-to-child transmission (MTCT) of HIV [1].

Unintended pregnancies are pregnancies that are unplanned or unwanted or mistimed [11]. Prevention of unplanned pregnancies is a crucial aspect of PMTCT, but the incidence of unplanned pregnancy remains high globally. For example, an estimated 35% of pregnancies in sub-Saharan Africa are unplanned [12]. Unintended pregnancy rate is higher among WLHIV compared to the general population [11, 13, 14]. Unplanned pregnancies among WLHIV range from 35% to 65% in sub-Saharan Africa and up to two thirds in South Africa

[13, 14]. Recent research among women aged 18-35 in South Africa suggests that 50%+ of pregnancies among women enrolled in PMTCT programs are unintended [14].

Unplanned pregnancies are associated with increased risk of maternal depression and stress as well as increased risk of adverse birth outcomes such as preterm delivery and premature rupture of membranes [11]. A study conducted in South Africa found an increased risk of elevated viral load with lower levels of pregnancy intendedness among women initiating ART during pregnancy [14]. Unplanned pregnancies are also linked to risky behaviours such as substance abuse, delays in entering antenatal care (ANC), and lower levels of breastfeeding [14].

Findings from a study conducted among South African women on ART suggest that the prevalence of contraceptive use among WLHIV ranges from 25-50% [15]. Contraceptive use also changes over time [15]. Specifically, there is a decrease in contraceptive use over time [15]. There is often discordance between fertility intentions and contraceptive use among WLHIV. Approximately 30 to 40% of WLHIV who do not want children or are ambivalent do not use any method of contraception [15]. This suggests gaps in routine care and missed opportunities to improve family planning services for WLHIV.

With adherence to ART, the risk of MTCT is close to zero [1, 16]. Given the high incidence of unplanned pregnancies, the discordance between fertility intentions and contraceptive use, and the potential implications of repeat pregnancies, we need a better understanding of maternal factors associated with repeat pregnancies, and how repeat pregnancies are affected by contraceptive use and fertility intentions. Currently, we do not have a clear understanding of future fertility intentions and contraceptive use among WLHIV and their influences on repeat pregnancies. The lack of conclusive evidence and complexity of future fertility intentions and contraceptive use leave room to explore the relationships mentioned above.

Rationale

As a result of the scale-up of PMTCT coverage and successful introduction of universal ART coverage, paediatric HIV infections have been significantly reduced. However, there is limited evidence evaluating the effect of fertility intentions and contraceptive use. Examining the effect of contraceptive use and fertility intentions on repeat pregnancies will highlight missed opportunities to improve family planning services. In light of the above, there is a clear need for more research that explores the association between pregnancy intentions, contraceptive use and repeat pregnancies. Also, associations within subgroups such as age, socio-economic status and level of education are needed to identify women who are at the highest risk. This research is crucial in evaluating family planning services provided in the PMTCT framework and general adult ART services.

Study Aims and Objectives

The proposed study aims to investigate the association between future pregnancy intentions, contraceptive use and repeat pregnancies in a cohort of ART initiated WLHIV who were followed through 36-60 months postpartum.

The specific objectives are:

1. To describe the incidence of repeat pregnancies
2. To explore associations between demographic characteristics and repeat pregnancies
3. To examine the association between repeat pregnancies and i) future fertility intentions and ii) contraceptive use
4. To investigate the association between a composite measure of future fertility intentions and contraceptive use with repeat pregnancies.

Methods

Study Design

The proposed study is a secondary data analysis of the Maternal and Child Health – Antiretroviral Therapy (MCH-ART) randomised controlled trial (https://clinicaltrials.gov/ct2/show/NCT01933477). Details regarding the MCH-ART study are available elsewhere [17]. Briefly, the trial compared different models for delivering HIV care to WLHIV during the postpartum period. A total of 471 women were enrolled into the trial and were followed postpartum, and an additional follow-up visit was conducted at 36-60 months postpartum for the "Long-term Adherence and Care Engagement" (LACE) study.

Analysis set

The proposed study will include all women enrolled in the postpartum follow-up as part of the MCH-ART trial.

Study setting

The parent study, MCH-ART, took place at the Gugulethu Midwife Obstetric Unit (MOU), where the team has a long history of delivering HIV care and treatment services. LACE was set at the Gugulethu Community Health Care Center (CHC), Cape Town, in the same site as the parent study. The CHC has provided PMTCT services since 2001.

Approximately 350 000 people access the facility [17]. The uptake of ANC is consistently greater than 95% [17]. The facility serves a population with high levels of poverty, low education levels, and a high burden of HIV [18]. Approximately 60% of the population live in informal housing. In 2015, 33% of the women attending ANC were HIV positive [18]. PMTCT services are integrated into ANC services as per South African national guidelines. All women are routinely tested for HIV during their first ANC visit and undergo pre- and post-test counselling. Women are referred to general adult ART services during the post-partum period.

Study Population

This analysis will include all women enrolled into postpartum follow-up for the MCH-ART trial, regardless of attendance at the LACE follow-up visit. Importantly, all women had initiated ART during pregnancy. Mother-infant pairs were enrolled within approximately 28 days post-partum and attended follow-up visits at 6 weeks and 3, 6, 9, 12 and 18 months post-partum. A subset attended the LACE study visit at 36-60 months postpartum.

Inclusion criteria

- Age ≥18 yrs.
- Enrolled in postpartum follow-up for the MCH-ART study
- Initiated ART during pregnancy
- Provided informed consent

Exclusion criteria

- Withdrawn from the MCH-ART study
- Known maternal death during study follow-up
- Unable to provide consent

Data collection

The proposed study will use data collected from mothers enrolled in the postpartum follow-up as part of the MCH-ART trial.

a. Enrolment Questionnaires

Women were enrolled in the study when entering ANC. Standardized questionnaires were completed to assess demographics (including age, socio-economic status, level of education) and medical history. Pregnancy intentions were assessed at enrolment using the validated 6-item London Measure of Unplanned Pregnancy (LMUP) tool. The range of possible scores sums from 0-12. Scores were categorised into unplanned (0-3), ambivalent (4-9) or planned (10-12) according to published scoring guidelines [19]. Future pregnancy intentions and

contraceptive use were also assessed at enrolment using a standardized questionnaire. All questionnaires were administered by trained interviewers in participants' home language (isiXhosa).

b. Assessment of future fertility intentions and contraceptive use

A standardised questionnaire was administered to assess future pregnancy intentions and contraceptive use at enrolment as well as the 12 months visit and 36-60 months visit. Only the assessment at the 12 months visit was used for this analysis. Future fertility intentions were thus assessed before any repeat pregnancy. Future pregnancy intentions were categorised as below;

- Wants to have a child in the next 12 months
- Wants to have a child sometime in the future
- Does not want to have a child in the future
- Unsure about whether or not wants to have a child in the future

For this analysis the categories "wants to have a child in the next 12 months" and "wants to have a child sometime in the future" have been combined to "wants a child in future" (table 2).

The history of contraceptive use was assessed by asking about the method of family planning during the last 12 months before the first pregnancy. Contraceptive use was thus assessed before any repeat pregnancy. Categories included: the oral contraceptive pill, 2 months injectable, 3 months injectable, intrauterine device (IUD), female sterilization, male sterilization and female/male condom. This analysis uses contraceptive use reported at 12 months postpartum. Contraceptive use is be defined as 'none' vs 'any'.

c. The Abstraction of routinely collected clinical information

In the parent study, information about subsequent pregnancies including date of delivery and delivery outcomes were requested from the Western Cape Provincial Data Centre. The Data

Centre stores data from all public sector facilities in the Western Cape. Data are linked across facilities using unique patient identifiers. Repeat pregnancy data from non-HIV services were excluded. Additional information was abstracted from the MOU and hospital records as required.

Table 1. Schedule of measurements to use in the proposed study

	Enrolment visit 1st Antenatal visit	**Phase 3** 12 months post-partum	**LACE** 36-60 months post-partum
Questionnaires			
Demographic and medical history	x		
Family planning use		x	
Future Fertility Intentions		x	
Unplanned pregnancy assessment	x		
Clinical data abstraction			
Antenatal and PMTCT information for subsequent pregnancies			x

Table.2 Variables to be included in the analysis

Variable	*Scale*	*Categories*
Maternal Demographics		
Age (years)	continuous	Quartile category proportions
	Categorical - ordinal	<24, 24-29, 30-39, 40+
Education	Categorical-binary	Finished high school, did not finish high school
Employment status	Categorical - binary	Employed, unemployed
Socio-economic status	Categorical-ordinal	Low, medium, high
Relationship status	Categorical-binary	Married/cohabitating, not married/not cohabitating
Gravidity	Categorical-ordinal	1, 2, ≥3
Parity	Categorical - ordinal	0, 1, ≥2
HIV		
Viral load (copies/ml)	Categorical - Ordinal	<50, 50-1000, >1000
Family planning and reproductive intentions		
Future Fertility intentions	Categorical-nominal	Wants a child in future, unsure, doesn't want a child in future
Unplanned pregnancy assessment	Categorical-nominal	unintended, ambivalent, intended
Contraceptive use	Categorical - binary	Some, none
Obstetric outcomes		
Birth outcomes	Categorical - binary	Repeat pregnancy, no repeat pregnancy

Data Management and Analysis

Data Management

Data collected in the parent study (MCH-ART) and the sub-study LACE was entered into a custom designed Microsoft access database, maintained in a firewall protected UCT server with nightly back-ups. The study database was password protected following standard password safety procedures. All study records do not contain participants' names or personal identifiers. Routine data was stored in a separate password protected database using only participant study identification numbers. The data used for this proposed study will be stored on a password protected computer accessible only to the researcher.

Data Analysis

Data will be analysed using STATA Version 15.0 (Stata Corporation, College Station, Texas) or R (Gnu Project). To describe the data, continuous variables will be summarised using the median and IQR. Categorical variables will be summarised using proportions/frequency percentages. Chi-square test will be used to compare proportions and rank-sum test for median values.

The incidence rate of repeat pregnancies will be calculated with a 95% confidence interval (CI). Crude rates (CR) will be compared as incident repeat pregnancy rate ratios (RR). (Objective 1). Kaplan Meir survival analysis will be used to examine associations between maternal characteristics and repeat pregnancy (objective 2). Kaplan Meier survival analysis will be used to estimate failure rates (occurrence of repeat pregnancies) by future fertility intention categories and contraceptive use categories (objective 3). The log rank test will be used to compare survival curves. Proportional hazards model will be used to compare the association between composite measure and repeat pregnancy (objective 4). Potential confounders or mediators will be examined before model building. Multivariate models will

include all covariates with a significant effect or influence on associations with outcome. Standard methods will be used for model diagnostics.

Ethical considerations

The parent study was approved by The University of Cape Town Faculty of Health Sciences Research Ethics Committee (UCT-HREC; REF: 451/2012), the Columbia University Medical Center Institutional Review Board (CUMC-IRB) and the research oversight body of the provincial government of the Western Cape Department of Health. The LACE sub-study was approved by UTC-HREC (REF: 866/2016). Ethical approval for this proposed secondary analysis will be sought from UCT-HREC.

Informed consent

For the MCH-ART and LACE studies, all women provided written informed consent in their home language, predominantly isiXhosa. Participants consented to the abstraction of their data from routine clinical records. This proposed study will analyse data collected during the enrolment and follow-up study visits as well as data already abstracted from routine clinical records per consent provided during the MCH-ART and LACE studies.

Privacy and confidentiality

Analysis in the proposed study will not include personal identifiers. The proposed study will ensure confidentiality by not reporting on individual participants or any variable that can be linked to an individual participant.

Risks and benefits

A description of potential risks and benefits, both indirect and direct, within the MCH-ART study have been provided and approved by UCT-HREC (REF: 451/2012)
This proposed study introduces minimal risks primarily due to the loss of confidentiality. However, measures have been previously implemented in the parent study and LACE follow-

up visit to ensure confidentiality. All data included in this analysis and the results presented will include no personal identifiers and the data will be securely stored, as described above. There are no direct benefits to study participants.

However, identifying the association between pregnancy intentions, contraceptive use and repeat pregnancies has the potential to yield indirect benefits. Increasing knowledge of the impact of pregnancy intentions and contraceptive use on repeat pregnancies may be important in evaluating the integration of family planning services into PMTCT and shed light on missed opportunities to improve family planning services for WLHIV. This may considerably benefit the study population as well as other WLHIV in lower middle income countries (LMICs).

Participant compensation

Since the proposed study involves only secondary data analysis, participants will not receive compensation. Participants received compensation for participating in the parent study and LACE sub-study. Participants received R150 in grocery vouchers, transport costs, and refreshments at study visits, and an educational gift for their child valued up to R100.

Dissemination of Results

The findings of this proposed study will be valuable in evaluating PMTCT programmes and general ART services in South Africa. The manuscript from this analysis will be published in a peer-reviewed journal. This way, relevant stake holders such as the Department of Health, and researchers in the same field will have access.

Study Timeline

	Aug' 2019	**Sept' 2019**	**Oct' 2019**	**Nov' 2019**	**Dec' 2019**	**Jan' 2019**	**Feb' 2019**
Protocol							
Literature Review							
Merge and clean data sets							
Analysis							
Draft Manuscript							
Final Manuscript & submission							

References

1. World Health Organization, *Towards the Elimination of Mother-To-Child Transmission of HIV*. 2010, World Health Organization. p. 10-13.
2. Myer, L., et al., *Impact of Antiretroviral Therapy on Incidence of Pregnancy among HIV-Infected Women in Sub-Saharan Africa: A Cohort Study.* PLOS Medicine, 2010. 7(2): p. e1000229.
3. Agadjanian, V. and S.R. Hayford, *HIV status, fertility intentions, and contraception in the era of expanded access to antiretroviral therapy: A case study of rural Mozambique.* Global Public Health, 2018. 13(5): p. 582-596.
4. Mekonnen, H. and F. Enquselassie, *Effect of antiretroviral therapy on changes in the fertility intentions of human immunodeficiency virus-positive women in Addis Ababa, Ethiopia: a prospective follow-up study.* Epidemiology and Health, 2017. 39.
5. Shiferaw, T., et al., *Fertility desire and associated factors among women on the reproductive age group of Antiretroviral treatment users in Jimma Town, South West Ethiopia.* BMC Research Notes, 2019. 12(1): p. 158.
6. Akelo, V., et al., *Determinants and Experiences of Repeat Pregnancy among HIV-Positive Kenyan Women--A Mixed-Methods Analysis.* PloS one, 2015. 10(6): p. e0131163-e0131163.
7. Iyun, V., et al., *Prevalence and determinants of unplanned pregnancy in HIV-positive and HIV-negative pregnant women in Cape Town, South Africa: a cross-sectional study.* BMJ Open, 2018. 8(4): p. e019979.
8. Kost, K. and L. Lindberg, *Pregnancy intentions, maternal behaviours, and infant health: investigating relationships with new measures and propensity score analysis.* Demography, 2015. 52(1): p. 83-111.

9. Heffron, R., et al., *Fertility Intentions, Pregnancy, and Use of PrEP and ART for Safer Conception Among East African HIV Serodiscordant Couples.* AIDS and behaviour, 2018. 22(6): p. 1758-1765.

10. Finocchario-Kessler, S., et al., *"We Weren't Using Condoms Because We Were Trying to Conceive": The Need for Reproductive Counseling for HIV-Positive Women in Clinical Care.* AIDS Patient Care and STDs, 2012. 26(11): p. 700-707.

11. Omani-Samani, R., et al., *Impact of Unintended Pregnancy on Maternal and Neonatal Outcomes.* The Journal of Obstetrics and Gynecology of India, 2019. 69(2): p. 136-141.

12. Sedgh, G., S. Singh, and R. Hussain, *Intended and Unintended Pregnancies Worldwide in 2012 and Recent Trends.* Studies in Family Planning, 2014. 45(3): p. 301-314.

13. Adeniyi, O.V., et al., *High rate of unplanned pregnancy in the context of integrated family planning and HIV care services in South Africa.* BMC Health Services Research, 2018. 18(1): p. 140.

14. Schwartz, S.R., et al., *High Incidence of Unplanned Pregnancy after Antiretroviral Therapy Initiation: Findings from a Prospective Cohort Study in South Africa.* PLOS ONE, 2012. 7(4): p. e36039.

15. Towriss, C.A., et al., *The injection or the injection? Restricted contraceptive choices among women living with HIV.* Sexual and Reproductive Health Matters, 2019. 27(1): p. 1628593.

16. Mandelbrot, L., et al., *No Perinatal HIV-1 Transmission From Women With Effective Antiretroviral Therapy Starting Before Conception.* Clinical Infectious Diseases, 2015. 61(11): p. 1715-1725.

17. Myer, L., et al., *Optimizing Antiretroviral Therapy (ART) for Maternal and Child Health (MCH): Rationale and Design of the MCH-ART Study.* Journal of acquired immune deficiency syndromes (1999), 2016. 72 Suppl 2(Suppl 2): p. S189-S196.

18. Myer, L., et al., *Plasma viraemia in HIV-positive pregnant women entering antenatal care in South Africa.* Journal of the International AIDS Society, 2015. 18(1): p. 20045.

19. Barrett, G., S.C. Smith, and K. Wellings, *Conceptualisation, development, and evaluation of a measure of unplanned pregnancy.* Journal of Epidemiology and Community Health, 2004. 58(5): p. 426.

SECTION B: LITERATURE REVIEW

Objective of literature review

This section provides a review of existing literature regarding future fertility intentions, contraceptive use and repeat pregnancies among women living with HIV (WLHIV). Fertility intentions and contraceptive use are presented as predictors of repeat pregnancies. In addition, this review summarises relevant knowledge related to trends and determinants of future fertility intentions and contraceptive use. These determinants are, inter alia, age, parity, and relationship status. This review identifies knowledge gaps and highlights research needs. Given that this dissertation uses data from a cohort of women in South Africa, this literature review includes only studies that were conducted in sub-Saharan Africa. Where appropriate, tables are used to summarise the characteristics and results of selected quantitative studies.

Methodology

Literature for this review was gathered from online peer reviewed journals. PubMed (Medline database) was searched for relevant literature, and reference lists were checked for additional publications. The search terms are listed below:

HIV: Human immunodeficiency virus (HIV), Acquired Immunodeficiency Syndrome (AIDS), Mother-to-Child Transmission (MTCT), vertical transmission, Prevention of Mother to Child Transmission (PMTCT), Perinatal infections,

Pregnancy intentions: pregnancy intentions, fertility intentions, reproductive intentions, future fertility intentions

Contraceptives: contraceptive use, family planning, birth control

Repeat pregnancy: repeat pregnancy, subsequent pregnancy, multiple pregnancies

Location: Sub- Saharan Africa,

We restricted the search to English language publications. No restrictions were made based on study design.

Many studies focused on predictors of future fertility intentions and contraceptive use. Four studies included the incidence of pregnancy as an outcome. None of the studies found specifically investigated the impact of fertility intentions and contraceptive use on repeat pregnancies. The studies included are described table 1.

Trends and determinants of fertility intentions

Trends

Much of the research has focused on fertility intentions related to the current or most recent pregnancy. Generally, fertility intentions are categorised into three categories in the literature: not wanting more children, unsure and wanting more children. The majority of the studies reporting the prevalence of fertility intentions are cross-sectional. The sample populations in these studies are comparable, and characteristics are detailed in tables 2 and 4. The median age range is 29– 33 years for all studies. In all studies, the majority of women had 2 or more children and had low socio-economic status [1-9]. All studies included a group of women who had initiated antiretroviral therapy (ART). Across studies, the majority of the women had disclosed their HIV status to their partners, except for a study conducted in Cameroon which reported that 69% of women had not disclosed their HIV positive status to their partner.

In general, the prevalence of not wanting more children ranges widely in the literature, from 45% in Cameroon and Uganda [2], to 71% in South Africa [3] and 95% in Malawi [4]. Other studies report a prevalence between these estimates [5-8, 10]. The prevalence of wanting more children ranges less widely, from 29% in South Africa [3] to 55% in Uganda [2].

This review identified three longitudinal studies that reported the prevalence of fertility intentions. Studies conducted in Ethiopia and South Africa included pregnant women who were not aware of their HIV status at baseline. In these studies, the prevalence of wanting children ranged from 32.9% in South Africa to 40.8% in Ethiopia at the beginning of the study, and 28.0% in South Africa to 48.3% in Ethiopia at 12 months follow up during the pre and postnatal period [7, 11]. The prevalence of wanting children was also similar among non-pregnant women in a study conducted in Malawi, with 29% of women reporting that they wanted children [12].

Determinants of fertility intentions

Intuitively, HIV status and ART use should affect fertility intentions due to improved health and sexual desire [13]. Interestingly, among a sample of ART initiated women aged 21 years or older in Cameroon, women's subjective perception of their physical health-related quality of life (HRQL) influenced their fertility desires [1].

The desire to have children typically declines immediately after knowledge of HIV status [7, 11]. In a cohort of ART naïve women in Malawi, future desire to have children declined from 33% to 15 % ($p<0.0001$) after knowledge of HIV positive results and remained constant over the one-year follow-up period [14].

There are conflicting results regarding the association between knowledge of a partner's HIV-positive status, one's own HIV status and ART use. Results from a cohort of 1766 monogamously married couples in Malawi reported that men and women who know their partner's HIV-positive status are twice as likely to not want more children compared to those who did not know, regardless of ART use [15]. However, a cohort of 1855 women in Ethiopia showed no correlation between knowledge of a partner's HIV-positive status and fertility intentions [16].

A summary of Demographic and Health Surveys (DHS) conducted in nine African countries revealed no statistically significant association between knowledge of own HIV-positive status and the odds of wanting more children. In these studies WLHIV did not differ from HIV negative women in terms of their desire for more children [17]. Conversely, in Uganda, WLHIV were less likely to desire children at present and in the near future compared to HIV negative women (8% vs 49%; $p<0.001$) [18, 19]. Furthermore, WLHIV were also less likely to change from not wanting children at baseline to wanting children at 12 months compared to their HIV negative counterparts [12]. The differences in results across these studies could be due to confounding factors such as age and gender. For example, the study conducted in Malawi included both men and women in monogamous couples, which may differ from results observed among women.

The desire to have children is consistently reported to be higher among ART initiated women compared to ART-Naïve women [1, 7, 16]. For example, women on ART were more likely to change from not wanting children to wanting children at 12 months follow up in a study conducted in Ethiopia [7]. In South Africa, the duration on ART was reported to be associated with fertility intentions among females. In this study, being on ART for 12 months or more was associated with a 3-fold increased likelihood of desiring children compared to being on ART for less than 6 months [3]. On the contrary, findings from a cohort of monogamous couples in Malawi suggest that there is no difference in fertility intentions between ART-nitiated and ART-naive participants [15]. This may be due to differences across populations.

Age and the number of live children are very well documented as predictors of fertility intentions. Associations with these factors were observed in multiple contexts [1, 3, 6, 7, 16, 19, 20]. All studies described the reproductive age as 18-49 years. In most studies, younger age was associated with an increased desire to have more children. A longitudinal

study conducted in Malawi investigating the change from not wanting more children at the beginning of the study to wanting more children at the end of 12 months follow up among non-pregnant women found that women <20 years old were more likely to change from not wanting children to wanting children compared to women aged 30 years [12]. In this study, older women were more likely to change to not wanting more children [12]. Conversely, a study conducted in Ghana shows an increased desire to have children among women aged 30-39 years compared to women aged 18-24 years [20].

The desire to have children typically declines with an increasing number of living children. More specifically, having more than two living children and having more than two minor children in the household were associated with decreased odds of desiring more children compared to having no living children and having no minor children in the household in a study conducted in Uganda [2]. Additionally, women with two or more living children were less likely to change from not wanting children to wanting children compared to women without children [7, 12]. Women with more living children were more likely to change to not wanting more children [12].

Much of the literature highlights the importance of couple communication around fertility intentions. For example, a male partner's fertility intentions are found to impact women's fertility intentions [2, 19]. In addition, disclosure of an HIV positive status to one's partner is associated with an increased desire to have children [11]. Conversely, partners may choose to not want children after disclosure. Being in a serodiscordant couple is associated with a decreased desire to have children [11]. Male partner support is also important in women's desire to have more children. For example, male partner involvement in the mother and child care continuum has been reported to be associated with an increased likelihood to desire more children among prenatal and postnatal women in South Africa [11].

Although inconclusive, there is evidence suggesting that marital status may affect fertility intentions. In studies conducted in Ethiopia and Malawi, marital status was identified as a predictor of fertility intentions. Specifically, single and married women were more likely to report a desire to have children compared to divorced/widowed women [4, 7]. Divorced and widowed women are reported as being less likely to want children compared to single women among both pregnant and non-pregnant women of reproductive age [3, 6, 16]. However, an increased desire to have children has been observed among single women compared to married women in Kenya [6], whilst no difference was observed between married and single women in Ethiopia [16]. Marital status has also been shown to not influence changes in fertility intentions from not wanting children to wanting children in Malawi [14]. The duration of the relationship possibly modifies the association between being in a relationship and fertility intentions compared to being single. In a study conducted in South Africa, being in a relationship for less than 5 years increased the odds of wanting a child compared to not being in a relationship [3].

Additionally, having some level of education is associated with an increased likelihood to desire a child [16]. Being well informed about HIV disease was also associated with wanting a child [1], and information about family planning is associated with fertility intentions [2, 11]. In South Africa, a time varying covariate associated with wanting more children is lower levels of family planning knowledge. Health care providers have an important role in educating women about family planning methods and opening up the conversation about fertility intentions among HIV positive women. Receiving counselling from a health care provider about future pregnancy has been observed to be associated with fertility intentions over the prenatal and postpartum period [2, 11].

Synthesis

Taken together, the findings summarized above give insights into the trends and determinants of fertility intentions. However, the trends of fertility intentions vary widely among studies. These may be due to differences in the timing of measurement or differences in the context. There are conflicting results on the relationship between knowledge of a partner's HIV-positive status, knowledge of one's HIV-positive status, ART use and marital status and fertility intentions. These discrepancies may be due to the sample sizes, as well as differences in study populations and study timing. More longitudinal studies are needed to better understand the trends and predictors of fertility intentions (Table 2). Understanding trends and determinants of fertility intentions will help identify the need for contraceptive use, including the current need as well as unmet needs for contraceptives. This information may be useful when designing reproductive services for HIV infected women.

Table 2. Overview of select studies that report on the prevalence of fertility intentions among WLHIV

Citation	Location	Study Population	Used Longinditudinal data	Prevalence of fertility intentions (%)
Atukunda; 2018	Uganda	Post-partum WHLIV≥18years	No	55% desired children
Haddad; 2015	Malawi	WLHIV seeking family planning services	No	95% did not desire more children
Marcelin; 2010	Cameroon	HIV + ART initiated women diagnosed for at least 3 months and are older than 21 years old	No	55% desired more children
Mayhew; 2017	Kenya	WLWH	Yes	71% did not desire more children
Mekonnen; 2017	Ethiopia	WLWH	Yes	Baseline: 41% desired children 12 months: 48.3% desired children
Myer; 2007	South Africa	HIV infected women and men	No	26% women desired more children 36% men desired more children
Ngugi at al;2016	Kenya	Sexually active women of 15-49 years	No	58% did not desire children in the future

O'shea et al; 2015	Malawi	HIV infected pregnant women on ART 18 – 45 years	No	1% desired additional pregnancy in next 2 years
Peltzer et al; 2019	South Africa	HIV infected pregnant women aged ≥18 years	Yes	Baseline: 33% indicated fertility intention 12 months: 28% indicated fertility intention

Trends and determinants of contraceptive use

Trends

Generally, contraceptive use is defined as the use of any short-term or long-term birth control method during reproductive years (18-49 years). The prevalence of contraceptive use ranges widely from 38% in Malawi [18] to 92% in Kenya [6]. Other studies report a prevalence in between these estimates [5, 8-10, 18, 21]. Contraceptive use is particularly low during the post-partum period [10].

There seems to be an increase in contraceptive use immediately following an HIV positive diagnosis. In a cohort in Malawi, for example, contraceptive use increased from 38% to 52% ($p<0.0001$) one week after diagnosis. In this study, contraceptive use remained constant during 3 months of follow up and then decreased over the one year follow up period to 46% [14]. In this study, however, it was not specified whether condom use referred to the last sex act or every sex act.

Determinants

Contraceptive use among WLHIV is particularly interesting in this era of universal ART coverage. Literature suggests changes in fertility intentions, increased sexual desire and sexual activity after ART initiation [13]. It is interesting to observe if ART initiation also affects contraceptive use and if that corresponds with the changing fertility intentions. However, definitions of contraceptive use are not standard making it difficult to compare results across different settings.

Evidence regarding the association between HIV status and contraceptive use is inconclusive. While several studies have argued that WLHIV have higher levels of contraceptive use than their HIV negative counterparts [4, 12, 17, 18], other research has shown no variation in contraceptive use by HIV status [5, 10, 22]. Results from a study in

rural Mozambique suggest a similar timing of contraceptive initiation as well as resuming contraceptive use between WLHIV and HIV-negative and women during the postpartum period [10]. Additionally, women in this study who did not initiate or continue using contraceptives before the end of the first year of birth were unlikely to use contraceptives at all.

Being younger is associated with a decreased likelihood of using contraception [15, 18]. However, in rural Mozambique, no association was observed between age and the initiation of contraceptive use among postpartum women [10]. The same study also shows that older women are more likely to use long-term contraceptive methods such as intrauterine devices compared to younger women [10]. However, it is unclear whether age is associated with the continuation of contraceptive use.

The dissonance between fertility intentions and contraceptive use is consistently echoed in the existing literature. In a cohort in rural Mozambique, HIV negative women who did not desire more children in the future were more likely to start using contraception earlier than women who desired more children or who were ambivalent. This pattern is not the same in WLHIV, however, with fertility intentions having no influence on contraceptive use [10]. This finding is supported by research conducted in Malawi [15] and Kenya [5]. The desire to cease childbearing does not seem to influence higher contraceptive uptake [15]. In a study conducted in Malawi, 95 % of women reported not wanting more children in the future, but only 16% reported using any form of birth control before their most recent pregnancy [18]. Across the literature, the majority of women who do not desire another child use condoms and short-term contraceptive methods [4, 8, 9, 14, 18]. In a study conducted in Malawi, a large proportion of women (24%) reported getting pregnant while using a form of family planning [14]. Women using condoms were more likely to report getting pregnant, suggesting a need to increase awareness and accessibility of safer contraceptive methods.

Knowledge of contraceptive methods and HIV disease are both associated with an increased likelihood of contraceptive use. A contraceptive knowledge assessment in Rwanda revealed that over 90% of WLHIV knew at least one form of contraceptive. In addition, approximately 70% of the women had discussed family planning with a health care provider after their recent pregnancy regardless of HIV status [18]. Women who received counselling from a health care provider about contraceptive use were more likely to initiate use early and to continue using contraceptives [10]. Moreover, the positive impact of HIV disease knowledge is greater among women who attend a family planning clinic compared to those who don't [18]. This highlights the unique opportunity that health care providers have to increase contraceptive uptake.

Similar to fertility intentions, couple communication is important in terms of contraceptive use. Couples who agree to not have children are more likely to use contraceptives during every sexual act [15]. The positive association between HIV disease knowledge and contraceptive use also seems greater among women who disclosed their status to their partner [10, 18]. Women in a Sero-discordant couple in a study conducted in Malawi were five times more likely to report consistent use of condoms compared to Sero-concordant positive partners [14]. Results were similar in a study conducted in Kenya [10].

Women with at least secondary school education and women who are married/cohabiting were more likely to report contraceptive use [5, 10]. Postpartum women who are divorced/widowed/ separated tend to use long-term contraceptive methods such as intrauterine devices more so than single/married/cohabiting women [10].

Low and inconsistent contraception use has implications for women's health. It raises questions as to whether this is due to structural gaps in reproductive health services for WLHIV. Unintended pregnancy is commonly cited as the consequence of low contraceptive use and dissonance between fertility intentions and current contraceptive use. In the existing

literature, the prevalence of unintended pregnancies ranged from 40% in Kenya [6] to 75% in Malawi among women who are aware of their HIV-positive status [8]. In Malawi, the prevalence was higher among WLHIV at 49% compared to 37% in HIV uninfected women (p=0.004) [8].

Younger women are repeatedly reported as being at higher risk of unintended pregnancies [9, 22]. Other factors associated with an increased risk of unintended pregnancies are being single or divorced, the number of living children and being on ART for longer than two years [9, 22]. Having a tertiary education is associated with lower odds of unwanted pregnancy and mistimed births [9, 22].

Rucinski et al studied unmet contraceptive needs in non-pregnant WLHIV on ART aged 13-35 years in South Africa. In this study, 50% of the women had a high predicted probability of unmet contraceptive needs and this unmet need increased over time [21]. In this cohort, one in 10 women were predicted to have unmet contraceptive needs and thus were at a higher risk of unintended pregnancy [21]. Limited uptake and discontinuation of contraceptives may be due to the fear of side effects in the case of hormonal methods and structural barriers such as accessibility and long waiting times [21, 23]. This may impact the incidence of pregnancy.

Synthesis

Overall, the trend of contraceptive use varies widely across studies. Most studies echo the dissonance between fertility intentions and contraceptive use. However, there is a lack of consistency in the definitions of contraceptive use as shown in table 3. Most studies do not specify whether contraceptive use refers to the last sexual act or consistent use. Furthermore, more longitudinal studies are needed to better understand the trends and predictors of contraceptive use.

Table 3. Overview of select studies that report on the prevalence of contraceptive use among WLHIV

Citation	Location	Study population	Used longitudinal data	Definition of contraceptive use	Prevalence of contraceptive use (%)
Agadjanian & Hayford; 2018	Mozambique	Postpartum women attending rural maternity clinics	No	Use of any contraceptive at least once since focal birth	41.4%
Elul et al; 2009	Rwanda	Postpartum women enrolled in PMTCT program	No	Use of any family planning method at time of data collection	54%
Hoffmann; 2008	Malawi	Non-pregnant women diagnosed with HIV at enrolment	Yes	Use of any contraceptive method at time of data collection	38%
Rucinski et al; 2018	South Africa	Non pregnant WLHIV on ART age 13-35	Yes	Not specified	43.2%

Trends of pregnancies and repeat pregnancies

Few studies have investigated the incidence of pregnancies among WLHIV. The occurrence of pregnancy among WLHIV may be associated with an increased risk of virologic failure, maternal complications, maternal death and low retention in care [13, 24]. The MTCT risk is highest in low resource settings that fail to retain women through the HIV care cascade. A study conducted among WLHIV of reproductive age predicted the incidence of pregnancy over 10 years after initiation of ART in West Africa. Eight countries were

included in the analysis: Benin, Burkina Faso, Cote d'Ivoire, Gambia, Guinea-Bissau, Mali, Nigeria and Senegal [24]. In this analysis, the average crude incidence rate was 2.96 pregnancies per 100 women-years. The incidence rate of first pregnancy ranged from 1.31 to 3.46 pregnancies per 100 women-years in Guinea-Bissau and Burkina Faso respectively. Three countries had an incidence rate above 3 and five countries below 3 per 100 women-years. Another study investigating the incidence of pregnancy in seven African countries found a higher crude incidence rate of 7.8 incident pregnancies per 100 person years. The rate peaked at 21.68 pregnancies per 100 person years in Rwanda [13]. In Malawi, the incidence rate was 8.20 pregnancies per 100 women years [25]. The rate was much higher in another cohort of WLHIV in Malawi at 14 pregnancies per 100 person years [12]. In this study, there were 120 total pregnancies (17%), including 100 first time pregnancies and 20 repeat pregnancies [12].

Factors associated with pregnancy occurrence

Timing of ART initiation and clinical disease stage affect the rate of incident pregnancies. In a study conducted in West Africa, women at an advanced HIV clinical stage, WHO stages III and IV, were less likely to report a pregnancy after ART initiation compared to women at a less advanced stage [24]. In this study, having a higher CD4 cell count at ART initiation increased the risk of first pregnancy. Results from a study of pregnant or recently post-partum women in South Africa also support the associations [13].

Multiple studies have consistently cited age as a predictor of incident pregnancy. In the same study in West Africa, younger women had a higher risk of experiencing a first pregnancy when compared to women aged 40-49 years. This was especially true among women aged 25-29 years, peaking at an estimated 5 pregnancies per 100 women-years [24]. In a study conducted in South Africa, women younger than 25 years had double the rate of

incident pregnancies compared to women aged 35 years and above. This was true for both ART initiated and ART naïve women. In this study, contraceptive use was associated with lower rates of pregnancy. This was largely due to hormonal methods. Condom use was associated with a higher rate of pregnancy compared to hormonal methods [13].

The risk of pregnancy has been consistently cited to decrease with increasing number of live children [13, 14]. In a study conducted in Malawi, HIV test results were associated with pregnancy incidence [14]. Women who reported wanting more children after receipt of HIV positive results had 2.2 times the pregnancy incidence rate [95%CI: 1.01 to 4.87] compared to those who reported not wanting more children in the future [14]. Overall, there is inconclusive evidence about the relationship between the incidence of pregnancy and each of marital status and disclosure of HIV positive status.

Conclusion: Areas for Further Research

Much of the existing literature focuses on predictors of fertility intentions and contraceptive use alone. Also, much of the existing literature is dated hence the need for further research. Five of the twenty-five papers included in this review are over 10 years old and only twelve are less than five years old. More research is needed to make meaningful conclusions about the predictors of pregnancies or repeat pregnancies among WLHIV. This research will contribute to the body of knowledge on the reproductive health of WLHIV and inform interventions that address the reproductive needs of WLHIV and evaluation of PMTCT programs.

References

1. Marcellin, F., et al., *Desire for a child among HIV-infected women receiving antiretroviral therapy in Cameroon: results from the national survey EVAL (ANRS 12-116).* AIDS Care, 2010. 22(4): p. 441-451.

2. Atukunda, E.C., et al., *Factors Associated with Pregnancy Intentions Amongst Postpartum Women Living with HIV in Rural Southwestern Uganda.* AIDS and Behavior, 2019. 23(6): p. 1552-1560.

3. Myer, L., C. Morroni, and K. Rebe, *Prevalence and Determinants of Fertility Intentions of HIV-Infected Women and Men Receiving Antiretroviral Therapy in South Africa.* AIDS Patient Care and STDs, 2007. 21(4): p. 278-285.

4. Haddad, L.B., et al., *Pregnancy prevention and condom use practices among HIV-infected women on antiretroviral therapy seeking family planning in Lilongwe, Malawi.* PloS one, 2015. 10(3): p. e0121039-e0121039.

5. Ngugi, E.W., et al., *Contraceptive practices and fertility desires among HIV-infected and uninfected women in Kenya: results from a nationally representative study.* Journal of acquired immune deficiency syndromes (1999), 2014. 66 Suppl 1(Suppl 1): p. S75-S81.

6. Mayhew, S.H., et al., *Fertility intentions and contraceptive practices among clinic-users living with HIV in Kenya: a mixed methods study.* BMC public health, 2017. 17(1): p. 626-626.

7. Mekonnen, H. and F. Enquselassie, *Effect of antiretroviral therapy on changes in the fertility intentions of human immunodeficiency virus-positive women in Addis Ababa,*

Ethiopia: a prospective follow-up study. Epidemiology and health, 2017. 39: p. e2017028-e2017028.

8. O'Shea, M.S., et al., *Effect of HIV status on fertility desire and knowledge of long-acting reversible contraception of postpartum Malawian women.* AIDS care, 2015. 27(4): p. 489-498.

9. O'Shea, M.S., et al., *Reproductive intentions and family planning practices of pregnant HIV-infected Malawian women on antiretroviral therapy.* AIDS care, 2016. 28(8): p. 1027-1034.

10. Agadjanian, V. and S.R. Hayford, *HIV status, fertility intentions, and contraception in the era of expanded access to antiretroviral therapy: A case study of rural Mozambique.* Global public health, 2018. 13(5): p. 582-596.

11. Peltzer, K., et al., *Fertility intentions of prenatal and postpartum HIV-positive women in primary care in Mpumalanga province, South Africa: a longitudinal study.* HIV/AIDS (Auckland, N.Z.), 2018. 10: p. 9-17.

12. Taulo, F., et al., *Fertility Intentions of HIV-1 Infected and Uninfected Women in Malawi: A Longitudinal Study.* AIDS and Behavior, 2009. 13(1): p. 20-27.

13. Myer, L., et al., *Impact of antiretroviral therapy on incidence of pregnancy among HIV-infected women in Sub-Saharan Africa: a cohort study.* PLoS medicine, 2010. 7(2): p. e1000229-e1000229.

14. Hoffman, I.F., et al., *The Year-Long Effect of HIV-Positive Test Results on Pregnancy Intentions, Contraceptive Use, and Pregnancy Incidence Among Malawian Women.* JAIDS Journal of Acquired Immune Deficiency Syndromes, 2008. 47(4): p. 477-483.

15. Dube, A.L.N., et al., *Fertility intentions and use of contraception among monogamous couples in northern Malawi in the context of HIV testing: a cross-sectional analysis.* PloS one, 2012. 7(12): p. e51861-e51861.

16. Asfaw, H.M. and F.E. Gashe, *Fertility intentions among HIV positive women aged 18–49 years in Addis Ababa Ethiopia: a cross sectional study.* Reproductive Health, 2014. 11(1): p. 36.

17. Mumah, J.N., A.K. Ziraba, and E.M. Sidze, *Effect of HIV status on fertility intention and contraceptive use among women in nine sub-Saharan African countries: evidence from Demographic and Health Surveys.* Global health action, 2014. 7: p. 25579-25579.

18. Elul, B., et al., *Pregnancy desires, and contraceptive knowledge and use among prevention of mother-to-child transmission clients in Rwanda.* AIDS, 2009. 23: p. S19-S26.

19. Joseph Davey, D.L., et al., *Difficult decisions: Evaluating individual and couple-level fertility intentions and HIV acquisition among HIV serodiscordant couples in Zambia.* PLOS ONE, 2018. 13(1): p. e0189869.

20. Laar, A.K., A.E. Taylor, and B.A. Akasoe, *HIV-seropositivity is not important in childbearing decision-making among HIV-positive Ghanaian women receiving antiretroviral therapy.* AIDS Care, 2015. 27(7): p. 870-875.

21. Rucinski, K.B., et al., *Longitudinal patterns of unmet need for contraception among women living with HIV on antiretroviral therapy in South Africa.* PloS one, 2018. 13(12): p. e0209114-e0209114.

22. Warren, C.E., et al., *Family planning practices and pregnancy intentions among HIV-positive and HIV-negative postpartum women in Swaziland: a cross sectional survey.* BMC pregnancy and childbirth, 2013. 13: p. 150-150.

23. Haider, T.L. and M. Sharma, *Barriers to Family Planning and Contraception Uptake in Sub-Saharan Africa: A Systematic Review.* International Quarterly of Community Health Education, 2013. 33(4): p. 403-413.

24. Burgos-Soto, J., et al., *Incidence of pregnancy after antiretroviral therapy initiation and associated factors in 8 West African countries.* Journal of acquired immune deficiency syndromes (1999), 2014. 67(2): p. e45-e54.

25. Homsy, J., et al., *Reproductive Intentions and Outcomes among Women on Antiretroviral Therapy in Rural Uganda: A Prospective Cohort Study.* PLOS ONE, 2009. 4(1): p. e4149.

Table 1. Description of studies included

Intext citation	First Author, year	Setting	Time of study	Study design and sample size (n))	Population	Outcome	Methods of outcome assessment	Findings
[10]	Agadjania & Hayford, 2018	Gaza Province, Mozambique	2012- 2013	Case Study, n = 285 (121 HIV +, 164 HIV -)	Postpartum women attending rural maternity clinics	Timing of contraceptive initiation and current contraceptive use	Standardized questionnaire	Higher education, religion and use of family planning counselling services associated with contraceptive use Fertility intentions, age, partnerships status, household material and parity not associated with contraceptive initiation or current contraceptive use.
[16]	Asfaw, 2014	Addis Ababa, Ethiopia	2012	Cross sectional study n = 1855	HIV+ women of reproductive age (18 – 49 years)	Fertility intentions	Interviewer administered structured questionnaire	ART use, age, marital status, parity, education associated with fertility intentions.
[2]	Atukunda, 2018	Mbarara, Uganda	2016 -2017	Secondary data analysis of RCT N=378	Post-partum WHLIV≥18years	Future pregnancy plans	Interviewer administered questionnaire	Desire to have children associated with partner's desires to have more children, referent pregnancy planned and higher household income. Increasing age, previous contraceptive use, and parity >2 associated with reduced odds of pregnancy intention.
[24]	Burgos-Soto, 2014	Benin Burkina Faso Cote d'Ivoire	Not specified	Retrospective cohort analysis	HIV infected women <50 years that	Incidence of pregnancy	Abstraction from regional database	Crude incidence of first pregnancy 2.9 per 100 person years

		Gambia Guinea-Bissau Mali Nigeria Senegal		n=29,425	initiated ART between Jan 1998 – Dec 2011			25-29 years had highest risk of pregnancy.
[15]	Dube, 2012	Karonga, Malawi	2008-2009	Cross-sectional analysis n =1766	Monogamous couples Men aged 15–59 years and women aged 15–49 years	Fertility intentions and contraceptive use	Demographic Census	Age, number of children and level of education positively associated with wanting less children HIV+ status associated with wanting to cease child bearing Contraceptive use not associated with HIV status, partner fertility desires. Couples agreeing to stop child bearing more likely to use any form of contraceptives.
[19]	Dvora, 2018	Lusaka, Zambia	1995 - 2012	Prospective cohort n=1029	Adult heterosexual Serodiscodant couples	Fertility intentions and HIV acquisition	Behavioural assessment and medical history questionnaires HIV testing Fertility intentions	Female fertility intentions associated with parity and partner fertility intentions Male fertility intentions associated with age, partner fertility intentions and previous partners' pregnancies. Seroconversion associated with desire to have more children, partner fertility intentions and couples agreement have more children.
[18]	Elul, 2009	Rwanda	April – May 2006	Cross sectional survey	Postpartum women	Pregnancy intentions	Interviewer administered	HIV + women less likely to report wanting more children

				n = 236 HIV+ e and 162 HIV-	enrolled in PMTCT program	Family planning knowledge and use	pretested close ended questionnaires	Low contraceptive use across both groups Number of ANC visits associated with contraceptive use
[4]	Haddad, 2015	Lilongwe, Malawi	August – December 2010	Cross sectional survey n= 200	WLHIV seeking family planning services	Fertility intentions Unintended pregnancy Contraceptive use / condom use	Interviewer-administered questionnaire	95 % did not desire future pregnancies 69% unintended pregnancies Higher education, older age, HIV negative partner and lower parity associated with consistent condom use
	Haider, 2013	Commentary on the barriers to contraceptive uptake in sub-Saharan Africa						
[14]	Hoffmann, 2008	Lilongwe, Malawi	December 2003 – January 2005	Prospective cohort n= 227	Women diagnosed with HIV at enrolment	Contraceptive use HIV status Pregnancy intentions	Voluntary HIV Testing Contraceptive use and pregnancy intention questionnaires	Knowledge of HIV+ status associated with decreased desire to have children Knowledge of HIV+ status associated with increased contraceptive use
[25]	Homsy 2008	Tororo and Busia Uganda	May 2003 – May 2004	Prospective cohort n= 733	HIV infected women started on ART	Reproductive intentions Pregnancy incidence	In-depth questionnaires	Pregnancy incidence rate: 8.20 per 100 women years 120 total pregnancies (17%), 100 first time pregnancies and 20 repeat pregnancies

						Family planning		33 % women with no desire to have children did not use contraceptive
[20]	Laar 2015	Southern Ghana	May 5 – June 30 2014	Cross-sectional study n= 318	HIV positive women aged 18 – 49 years	Fertility intentions	Interviewer administered questionnaires	Fertility intentions associated with age, HIV positive man, number of children Age 30-39 associated with increased desire to have children. Having <2 children associated increase in desire to have more children
[1]	Marcellin 2010	Cameroon	September 2006 and March 2007	National cross sectional survey n=1433	HIV positive women on ART <50 years old	Fertility intentions	National survey questionnaires	791 (55%) women desired to have children Good physical health, low CD4 cells <200 cell/mm^3, younger age, being married or in a free union, disclosure of HIV status to partner associated with desire for a child.
[6]	Mayhew, 2017	Kenya	October 2009–April 2010 and October 2011–April 2012	non-randomised pre-post intervention trial: mixed methods n= 240	WLWH	Fertility intentions and outcome [Family planning uptake	Interviewer administered questionnaires In depth interviews	High family planning uptake (92%) as well as unintended pregnancies (40%)
[3]	Myer, 2007	Cape Town, South Africa	August and November 2005	Cross-sectional study n=311	HIV infected women and men	Prevalence and determinants of fertility intentions	Semi-structured questionnaire	29% wanted children, 71% did not want children, and <1% unsure Increased fertility desire associated with male gender and younger age. Decreased

								fertility desire associated with having 2 children or more.
[13]	Myer, 2010	9 African countries not specified	February 2003-January 2007	Data analysis of MCH-ART RCT n=4531	pregnant or recently postpartum HIV-infected	Incidence of pregnancy	Standardised questionnaires	589 incident pregnancies 7.8 pregnancies per 100 person-years
[7]	Mekonnen, 2017	Addiss Ababa, Ethiopia	June 2012 and October 2013	Institution-based follow-up study n=360	WLWH	Change in fertility intentions	Interviewer-administered structured questionnaires	Changing from no desire for children to desiring children associated with ART initiation, marital status, disclosure of HIV status to partner, and family influence. Educational status, income, partner's desire to have children, partner's HIV test not associated with fertility intentions.
[17]	Mumah, 2014	Cameroon Ethiopia Guinea Kenya Lesotho Malawi Niger Rwanda Zimbabwe	Cameroon (2004 and 2011) Ethiopia (2005 and 2011) Guinea (2005 and 2012) Kenya (2003 and 2008/09) Lesotho (2004 and 2009)	Analysis of Demographic and health surveys (DHS)	Women of reproductive age: 15-49 years	Fertility intentions and modern contraceptive use	Standard DHS survey questionnaire	HIV status not significantly associated with in fertility intentions and contraceptive use

			Malawi (2004 and 2010) Rwanda (2005 and 2010) Niger (2006 and 2012) Zimbabwe (2005/06 and 2010/11)					
[5]	Ngugi, 2016	Nairobi, Kenya	2012 – 2013	Kenya AIDS indicator Survey n=3583	Sexually active women of 15-49 years	Fertility intentions and family planning FP) use	Interviewer administered household and individual questionnaires	68.2% FP use. 57.7% did not desire children in the future. 70.9% of those that did not desire kids were using FP. No difference if FP use between HIV infected and uninfected. Women with no HIV have higher odd AOR 2.27 of desiring children in the future.
[8]	O'Shea, 2015	Malawi		Cross sectional study n=630	Postpartum women ages 18-45 years	Fertility intentions and family planning use	Standardized survey questionnaire	HIV infected more likely to have no desire for children in the future (59% vs 26% $p<0.001$) HIV infected women more likely to report FP use Having >2 children and age over 30 associated with decreased desire for more children
[9]	O'Shea, 2016	Malawi	March – July 2014	Cross sectional study	HIV infected pregnant women on	Current pregnancy intention,	Face to face 30 minute survey	75 % of pregnancies were mistimed or unintended. Women on ART for 2 years or

				n=220	ART 18 – 45 years	contraceptive use at conception and future fertility intentions		more were more likely to have unintended pregnancies. 79% reported use of contraceptive. Condom was the most common contraceptive. 75% did not desire children in the future.
[11]	Peltzer, 2019	Mpumalanga, South Africa		Longitudinal study n=699	HIV infected pregnant women aged ≥18 years	Fertility intentions	Audio computer assisted self-interview	Time invariant covariates associated with fertility intentions; having no children (AOR 0.61 p <0.001), Serodiscodant couple or unknown partner status (AOR=0.76, p<0.01) having a partner with unknown/HIV-negative status, and disclosed HIV status to partner (AOR = 1.25, p<0.05) Time varying covariates associated with fertility intentions: less family planning knowledge (AOR = 0.84, p<0.001), counselling with health provider about future pregnancy (AOR=1.34, p<0.01), and male partner involvement (AOR = 1.01, p<0.01)
[21]	Rucinski, 2018	Johannesburg, South Africa	2009-2010	Modelling n=850	non pregnant HIV + women aged 18-35 years	Longitudinal patterns of unmet need for contraception.	Mathematical Modelling	50% women predicted to have high probability of unmet need 1 in 10 women at high risk of unintended pregnancy

[12]	Taulo, 2009	Blantyre, Malawi	January 2003 to May 2005	Prospective longitudinal study n=1606 (842 HIV- and 844 HIV +)	Women aged ≥18 years	Predictors of changes in fertility intentions	Standardized questionnaires	HIV infection significantly associated with changes in fertility intentions. Age, education, and coital frequency correlated with fertility intentions.
[22]	Warren, 2013	Swaziland	Not specified	Cross-sectional survey n=386 HIV + women n=483 HIV- women	Postpartum women 18-45 years	Family planning practices and fertility intentions	Standardized survey questionnaires	69.2% unintended pregnancies 37.9% did not want a child Younger women at increased risk of unintended pregnancy

SECTION C: MANUSCRIPT

Introduction

HIV continues to be a global public health priority, especially among women of reproductive age in Sub-Saharan Africa [1]. In South Africa, the HIV prevalence among first antenatal care visit attendees was 29% in 2017 [2]. The expansion of antiretroviral therapy (ART) services has decreased morbidity and mortality in the African setting. With this outstanding improvement in life expectancy, there is a growing focus on childbearing intentions among women living with HIV (WLHIV).

Childbearing among WLHIV is important for the following reasons. Firstly, pregnancy without precaution may lead to HIV transmission to spouse and infant. Secondly, HIV infection may increase the risk of pregnancy complications associated with maternal mortality [3]. Thirdly, fertility intentions may influence health behaviours such as health-seeking, ART use and substance use [4]. This highlights the importance of addressing reproductive needs of WLHIV.

In sub-Saharan Africa, the emphasis has been on the prevention of mother-to-child transmission (PMTCT) of HIV through peripartum ART. Shifting the focus to fertility intentions and contraceptive use can further reduce the risk of mother-to-child transmission (MTCT) and unintended pregnancies [5]. Evidence suggests that WLHIV have higher rates of unintended pregnancies compared to the general population [6-8]. Unintended pregnancy among WLHIV range from 35% to 65% in sub-Saharan Africa and up to two thirds in South Africa [7, 8]. In South Africa, more than 50% of women aged 18-35 years attending PMTCT programs report that their pregnancies were unintended [8].

To address this, the World Health Organisation (WHO) promotes a comprehensive PMTCT approach which includes preventing unintended pregnancies and preventing HIV among women of childbearing age [9]. Family planning (FP) is listed as a cost-effective method for decreasing the proportion of infants born with HIV [9]. WHO recommends integrating reproductive health services within PMTCT interventions and supporting WLHIV to make informed decisions about their reproductive health.

HIV care services are in a unique position to address the reproductive health needs of WLHIV following WHO's recommendations. In sub-Saharan Africa, there are increasing efforts to develop comprehensive PMTCT programs. However, evidence regarding the predictors of first pregnancy among WLHIV is inconclusive, and there are few data on factors influencing repeat pregnancies. To inform such

interventions, this study aims to investigate the effect of fertility intentions and contraceptive use on the occurrence of repeat pregnancies among WLHIV in Cape Town, South Africa. We examine the incidence of repeat pregnancies and predictors of repeat pregnancy.

Methods

Study Setting and Population

This secondary analysis uses data from the Maternal Child Health-Antiretroviral Therapy (MCH-ART) study (ClinicalTrials.gov NCT01933477), conducted at the Gugulethu Midwife Obstetric Unit (MOU) in Cape Town, South Africa [10]. Approximately 5000 women sought antenatal care (ANC) at the MOU in 2011. In 2013, 33% of the women attending ANC were HIV positive as per findings from the parent study [10]. The population attending the facility is characterised by high levels of poverty, low education levels, and a high burden of HIV.

Inclusion and Exclusion Criteria

As part of the MCH-ART study, women aged ≥18 years were enrolled when entering antenatal care. Women who initiated ART during pregnancy were followed through delivery, and women who opted to breastfeed were followed through 36-60 months postpartum. Women who withdrew from the parent study were excluded from this analysis.

Data Collection

Self-report data used in this study was collected using standardized questionnaires, including demographics, reproductive and medical history. Poverty categories were created using questionnaire data about employment status, household assets and type of housing. The categories were as follows; least disadvantaged, moderately disadvantaged and most disadvantaged. Pregnancy intentions were assessed at enrolment using the validated 6-item London Measure of Unplanned Pregnancy (LMUP) tool. Scores were summed for a total score ranging from 0-12. Scores were categorised into unplanned (0-3), ambivalent (4-9) or planned (10-12) according to published scoring guidelines [11]. Future fertility intentions and contraceptive use were assessed using questionnaires at enrolment as well as the 12 months visit and 36-60 month visit. This analysis uses future fertility intentions and contraceptive use data collected at the 12

months visit. Future fertility intentions appear in the following categories; doesn't want a child in the future, unsure and wants a child in the future. Current contraceptive use at 12 months postpartum is categorised into 'none' vs 'any' use. We created a composite variable of future fertility intentions and contraceptive use at 12 months postpartum, combining those who were unsure about wanting a child in the future with those who want a child in the future. The composite measure was categorised as follows; 'doesn't want child in the future and uses contraceptive', 'doesn't want child in the future and doesn't use contraceptive', 'wants child in the future and uses contraceptive' and 'wants child in the future and doesn't use contraceptive'.

Obstetric outcomes (previous and repeat pregnancies), mode and date of delivery were abstracted from the Western Cape Provincial Data Centre. This data center includes all public health facilities in the Western Cape. Data are linked across facilities using unique patient identifiers. Repeat pregnancy data from non-HIV services were excluded. Additional information was abstracted from the MOU and hospital records as required.

Data Analysis

Data were analysed using STATA Version 15.0 (Stata Corporation, College Station, Texas) or R (Gnu Project). To describe the data, we summarised continuous variables using medians and inter-quartile range (IQR). Categorical variables were summarised using frequencies and percentages. Chi square test was used to compare proportions across occurrence of repeat pregnancy vs no repeat pregnancy. The rank sum was used to compare median values.

The incidence rate of repeat pregnancies was calculated with 95% confidence interval (CI). Kaplan Meier survival analysis was used to examine associations between maternal characteristics and repeat pregnancy. Kaplan Meier survival analysis was used to estimate occurrence of repeat pregnancies by fertility intentions, contraceptive use, LMUP scores, and maternal sociodemographic characteristics. Fertility intentions and contraceptive use were assessed at 12 months postpartum, and LMUP and sociodemographic characteristics at entry into antenatal care. The log rank test was used to compare survival curves. Predictors of repeat pregnancies were examined using Cox proportional hazards models. Results were reported as crude and adjusted Hazard Ratios (HR) with 95% CI.

Table 1. Description of socio-demographic and reproductive health characteristics overall and by repeat pregnancy

Variable	Total sample – n (%)	Pregnancy		p-value
		Repeat Pregnancy – n (%)	No repeat pregnancy – n (%)	
Number of women	471	109 (23.14)	362(76.86)	
Demographics				
Median [IQR] age (years)	27.80 [24.47 – 32.25]	27.12 [23.12 – 30.99]	28.19 [24.73 - 32.91]	0.006
Age category				
18-24	137 (29.09)	40(36.70)	97(26.80)	0.010
25-34	278 (59.02)	64(58.72)	214(59.12)	
35-45	56 (11.89)	4(4.59)	51(14.09)	
Educational attainment				
Less than secondary	354 (75.16)	80 (73.39)	274 (75.69)	0.627
Completed secondary/any tertiary	117(24.84)	29 (26.61)	88(24.31)	
Employment status				
Unemployed	287 (60.93)	73 (66.97)	214 (59.12)	0.141
Employed	184 (39.07)	36(33.03)	148 (40.88)	
Poverty category				
Most disadvantaged	164(34.82)	41(37.61)	123(33.98)	0.676
Moderate disadvantaged	158 (33.55)	37(33.94)	121(33.43)	
Least disadvantage	149 (31.63)	31(28.44)	118(32.60)	
Relationship status				
Not married/cohabiting	278(59.02)	61(55.96)	217(59.94)	0.459
Married/cohabiting	193(40.98)	48(44.04)	145(40.06)	
Obstetric characteristics				
Parity				
0	87(18.47)	23(21.10)	64(17.68)	0.116
1	188(39.92)	50(45.87)	138(38.12)	
≥2	196(41.61)	36(33.03)	160(44.20)	
Fertility intentions and contraceptive use				
Unplanned pregnancy assessment at entry into antenatal care				
Unplanned	278(59.91)	58(54.72)	220(61.45)	0.447
Ambivalent	92(19.83)	23(21.70)	69(19.27)	
Planned	94(20.26)	25(23.58)	69(19.27)	
Contraceptive use at 12 months postpartum				
None	60(18.02)	19(22.89)	41(16.40)	0.182
Some	273(81.98)	64(77.11)	209(83.60)	
Future fertility intentions at 12 months postpartum				
Doesn't want a child in the future	244(63.05)	44(47.83)	200(67.80)	0.001
Unsure	107(27.65)	32(34.78)	75(25.42)	
Wants a child in the future	36(9.30)	16(17.39)	20(6.78)	

Results

Sociodemographic characteristics of the study subjects

A total of 471 WLHIV were included in this analysis (Table 1). The median age was 28 years [IQR: 24-32]; 75% had less than secondary level education, and most were unemployed. The majority of the women were neither married nor cohabiting.

Reproductive, obstetric, and fertility intentions of study subjects

At enrolment, 464 women completed the LMUP. Unplanned pregnancy was reported by 60% of the women; 20% were ambivalent and 20% reported a planned pregnancy. Of the women that reported fertility intentions at 12 months postpartum, 63 % (244 of 387) reported not wanting children in the future. Most of the women (82%; 273 of 333) reported some form of contraceptive use at 12 months postpartum. Of the women with data on fertility intentions and contraceptive use, 54% (179/333) of the women who reported not wanting children in the future also reported using some form of contraceptive. However, 16% of the women who reported not wanting a child in the future or were unsure reported not using any contraceptive at 12 months postpartum.

Table 1 also compares demographic and obstetric characteristics of women who had a repeat pregnancy compared to those that did not. Of the women who had a repeat pregnancy, 83% (76/92) reported not wanting children in the future or being unsure. Overall, 59% of the women who had a repeat pregnancy were between 25-34 years old. There was a significant difference between age categories, with older women being less likely to have a repeat pregnancy. Approximately 59% of women with repeat pregnancies were 25-34 years old compared to 5% aged 35 to 45 years. No association was observed between repeat pregnancies and other demographic characteristics, LMUP scores at enrolment, or contraceptive use at 12 months postpartum.

Incidence rate of repeat pregnancy

Overall, 109 repeat pregnancies were detected. The incidence rate of repeat pregnancy was 5.72 per 100 person years (Table 2). The incidence rate of repeat pregnancy appeared to increase with decreasing age, with a rate of 2.11 repeat pregnancies per 100 person-years in the 35-45 years category, 5.63 repeat pregnancies per 100 person-years in the 25-34 category and 7.56 repeat pregnancies per 100 person-years in the 18-24 years category. The incidence rate of repeat pregnancy did not differ according to contraceptive use at 12 months postpartum (8.12 repeat pregnancies per 100 person-years among women not using contraceptives, versus 5.68 per 100 person-years among those using contraceptives; p=0.18; Figure 1). However, the rate of repeat pregnancy differed across future fertility intention categories reported at 12 months postpartum (Figure 2). The highest rate of repeat pregnancy was observed among those who reported that they want a child in the future at 12.59 repeat pregnancies per 100 person-years and the lowest rate among those who reported that they do not want a child in the future at 4.31 repeat pregnancies per 100 person years (log-rank p<0.001).

Table 2. Crude incidence rates of repeat pregnancy per 100 person-years of observation, with 95% CIs according to women's demographic, socioeconomic, and reproductive characteristics.

Characteristics	Incidence rate (95% CI)	P-value Log-rank test
Overall	5.72 [4.74, 6.90]	-
Demographics		
Age category		
18-24	7.56 [5.54, 10.30]	
25-34	5.63 [4.40, 7.19]	
35-45	2.11 [0.88, 5.06]	0.01
Educational attainment		
Less than secondary	5.68 [4.48, 6.94]	
Completed secondary/any tertiary	6.17 [4.29, 8.89]	0.63
Employment status		
Unemployed	6.35 [5.05, 7.99]	
Employed	4.77 [3.44, 6.62]	0.14
Poverty category		
Most disadvantaged	6.23 [4.62, 8.53]	
Moderate disadvantaged	5.75 [4.16, 7.93]	
Least disadvantage	5.11 [3.59, 7.26]	0.68
Relationship status		
Not married/cohabiting	5.41 [4.21, 6.95]	
Married/cohabiting	6.19 [4.66, 8.21]	0.46
Obstetric Characteristics		
Parity		
0	6.76 [4.49, 10.17]	
1	6.66 [5.05, 8.78]	
≥2	4.43 [3.20, 6.14]	0.12
Reproductive Characteristics		
Unplanned pregnancy assessment		
Unplanned	5.12 [3.96, 6.62]	
Ambivalent	6.23 [4.14, 9.28]	
Planned	6.65 [4.49, 9.84]	0.45
Contraceptive use		
None	8.12[5.18, 12.73]	
Some	5.68 [4.45, 7.26]	0.18
Future fertility intentions		
Doesn't a want child in the future	4.31[3.31, 5.79]	
Unsure	7.67 [5.42, 10.84]	
Wants a child in the future	12.59 [7.72, 20.54]	0.00

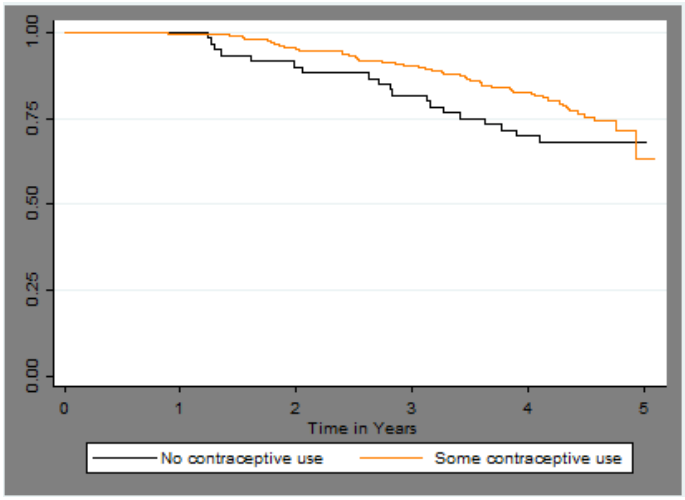

Figure 1. Kaplan Meier plot: Contraceptive use

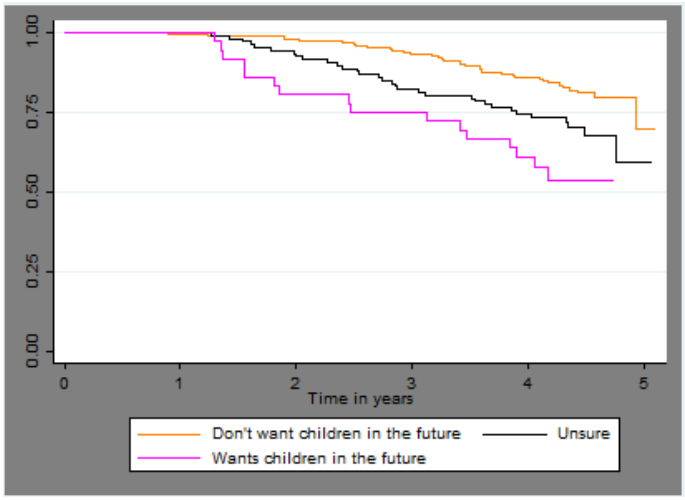

Figure 2. Kaplan Meir plot: Fertility intentions

Factors Associated with incident repeat pregnancies - Table 3

In univariate proportional hazard models (Table 3), only age and future fertility intentions reported at 12 months postpartum were identified as significant predictors of repeat pregnancies among WLHIV. These associations persisted in the multivariate model presented in table 3. Compared to women aged 18-24 years, women aged 35-45 years had a 74% decreased hazard of a repeat pregnancy (aHR:0.26 [0.09, 0.81]). Women who were unsure about having a child in the future had a 67% increased hazard of a repeat pregnancy compared to women who did not want a child in the future (aHR: 1.67 [1.00, 2.77]). There was a 3-fold increase in the hazard of a repeat pregnancy among women who wanted a child in the future compared to those that did not (aHR: 3.46 [1.83, 6.50]).

Table 4 presents a proportional hazard model with the composite measure of contraceptive use and future fertility intention reported at 12 months postpartum as a predictor. Overall, after adjusting for age, parity, employment, poverty category and relationship status; women who reported that they do not want a child in the future and reported the use of contraceptives had a 45% decreased hazard of a repeat pregnancy compared to women who reported that they do not want a child but reported no contraceptive use.

Table 3. Cox's proportional hazards models examining the association between demographic and reproductive characteristics and repeat pregnancies presented as HRs with 95% CIs.

	Crude associations		**Adjusted associations[1]**	
Characteristics	**HR (95%CI)**	**P-value**	**HR (95%CI)**	**P-value**
Age				
18-24	1	(ref)		
25-34	0.72[0.49, 1.08]	0.11	0.62 [0.38, 1.03]	0.06
35-45	0.26 [0.10, 0.66]	0.01	0.26[0.09, 0.81]	0.02
Educational attainment (ref less than secondary)				
Completed secondary/any tertiary	1.12 [0.73, 1.71]	0.60	1.06 [0.61, 1.83]	0.85
Poverty category				
Most disadvantaged	1	(ref)		
Moderate disadvantaged	0.91[0.58, 1.41]	0.68	0.83 [0.47, 1.45]	0.51
Least disadvantaged	0.81[0.51, 1.29]	0.38	0.81 [0.45, 1.45]	0.47
Relationship status (ref not married/cohabiting)				
Married/cohabiting	1.45[0.79, 1.67]	0.48	1.07 [0.64, 01.82]	0.79
Parity				
0	1	(ref)		
1	0.97[0.59, 1.60]	0.92	1.27[0.66, 2.42]	0.47
≥2	0.63[0.37, 1.06]	0.08	1.04[0.50, 2.17]	0.92
Unplanned pregnancy assessment at entry into antenatal care				
Unplanned	1	(ref)		
Ambivalent	1.26[0.78, 2.04]	0.93	1.18[0.66, 2.13]	0.57
Planned	1.30[0.81, 2.08]	1.10	0.92[0.51, 1.68]	0.79
Contraceptive use at 12 months postpartum (ref none)	0.68[0.41, 1.13]	0.14	0.722[0.42, 1.24]	0.24
Future fertility intentions at 12 months postpartum				
Doesn't want child in future	1	(ref)		
Ambivalent	1.87 [1.18, 2.94]	0.01	1.67[1.00, 2.77]	0.04
Wants child in the future	3.37[1.89, 5.98]	0.00	3.46[1.83, 6.50]	0.00

[1]Multivariate model was for all the covariates shown.

Table 4. Cox's proportional hazards models examining the association between composite measure of fertility/contraceptive use and repeat pregnancies reported at 12 months postpartum presented as HRs with 95% CIs.

	Crude Association		**Adjusted Association[2]**	
Composite measure	HR (95%CI)	P-value	HR (95%CI)	P-value
Doesn't want child in the future and doesn't use contraceptive	1	(ref)		
Doesn't want child in the future and uses contraceptive	0.52 [0.20, 0.87]	0.01	0.55 [0.32, 0.94]	0.03
Wants child in the future and uses contraceptive	0.84 [0.45, 1.56]	0.58	0.78 [0.42, 1.47]	0.45
Wants child in the future and doesn't use contraceptive	1.39 [0.61, 3.15]	0.42	1.35 [0.59, 3.13]	0.48

[2] Multivariate model was adjusted for age, parity, employment, poverty category and relationship status

Discussion

Our findings suggest an incidence of more than 5 repeat pregnancies per 100 person-years among WLHIV who initiated ART during pregnancy in South Africa. At 12 months postpartum, most women were using some form of contraceptives, and the majority did not desire children in the future. However, a large proportion of women who reported not wanting a child in the future or were unsure also reported not using any contraceptive method. No association was observed between contraceptive use at 12 months postpartum and repeat pregnancies, but age and future fertility intentions reported at 12 months postpartum were identified as predictors of repeat pregnancies. Wanting a child in the future and being unsure were both associated with an increased occurrence of repeat pregnancy. Nevertheless, almost half of the repeat pregnancies occurred among women who reported not wanting a child in the future.

Prior studies have reported a rate of approximately 3 to 14 incident pregnancies per 100 person years [12-15], but these studies investigated incidence of first pregnancy and not repeat pregnancy. As noted in other studies conducted in sub-Saharan Africa [12-15], our results indicated that younger women are at a higher risk of repeat pregnancy. In this study, 95% of the total repeat pregnancies occurred in women aged 18-34 (104/109). A study in 8 countries in West Africa [15] and a study in 7 African countries [12], also showed a significantly higher incidence of pregnancy among younger women compared to older women.

Our results concerning fertility intentions and repeat pregnancies are similar to those from a study conducted in Malawi [5], where women who wanted a child were more likely to be pregnant and the majority of the pregnancies occurred among women who reported no desire for a future child. Contrary to

other studies, contraceptive use was not associated with incident repeat pregnancy in this analysis. This may be due to discontinuation of contraceptive use and we did not measure contraceptive use continuation at 12 months postpartum. The prevalence of contraceptive use is high in this study. However, there may be a reliance on short-terms contraceptive methods e.g. condoms, which may have impacted the association between contraceptive use and repeat pregnancy. Other studies suggest a decreased risk of pregnancy with contraceptive use compared to no use [12, 16]. Specifically, hormonal methods are associated with a decreased incidence of pregnancy compared to condom use or no use at all [12].

The dissonance between future fertility intentions and contraceptiveat 12 months postpartum use observed in this study highlights the need to understand women's reproductive desires and contraceptive use. Understanding the reasons for this dissonance is important to improve reproductive health services integrated in the PMTCT framework or provided in routine care. This information is also crucial in evaluating family planning services provided in the PMTCT framework as recommended by WHO. In South Africa, 1 in 10 WLHIV were predicted to have a high probability of unmet FP needs that increase over time [8] . Low uptake of contraceptives may be due to structural gaps, social and cultural norms and gender empowerment issues [17]. To note, contraceptive use in this study was high at 12 months postpartum.

Routine HIV care services are in a unique position to regularly asses fertility intentions and contraceptive use to determine family planning needs of WLHIV. Regularly assessing reproductive health needs is important to prevent transmission to partners and unborn infants especially among viraemic women. Furthermore, it is an opportunity to provide needed support to prevent unintended pregnancies. Results from a study conducted in Kenya support the integration of family planning services into routine HIV care. Integration was associated with an increase in family planning uptake among WLHIV [16]. Sensitivity of providers to women's reproductive needs, providing family planning services at the same visit and accessibility of a reproductive health room as part of patient flow were identified as factors that encourage uptake of contraceptives [16].

A major strength of this study is the use of longitudinal data with long-term follow up. However, several limitations should be considered when interpreting findings from this analysis. First, contraceptive use and fertility intentions along with other behavioural outcomes were self-reported and are subject to

misclassification. To minimise social desirability bias, trained interviewers administered questionnaires in private. Second, contraceptive use and fertility intentions were assessed at 12 months postpartum and these may change overtime. Third, using routinely collected medical data may lead to underestimating the number of repeat pregnancies due to incompleteness. Fourth, the cohort was comprised of primigravida and multigravida women. It is unclear whether contraceptive use and fertility intentions would differ in women who have never been pregnant. Findings should be generalized to other settings with caution as the data used arise from a peri-urban setting and included women from a research study setting. However, we note that low levels of contraceptive uptake have been observed in many high burden settings in Sub-Saharan Africa.

Conclusion

We have demonstrated that age and fertility intentions affect the incidence of repeat pregnancies among WLHIV in Cape Town, South Africa. Future research that includes changes in fertility intentions and contraceptive use over time is needed to properly estimate the impact on occurrence of repeat pregnancies. As women's health and life expectancy significantly improve after initiating ART, routine screening of future fertility intentions and availability of safe contraception methods will be critical in ensuring the reproductive health needs of WLHIV are met and unintended pregnancies are averted. Understanding the dynamics of fertility among WLHIV is crucial when designing programs integrating reproductive health services into routine HIV care.

References

1. UNAIDS, *Global HIV & AIDS statistics — 2019 fact sheet.* 2019.
2. Woldesenbet, S.A., et al., *The 2017 National Antenatal Sentinel HIV Survey, South Africa,*, N.D.o. Health, Editor. 2019.
3. Brittain, K., et al., *Long-term effects of unintended pregnancy on antiretroviral therapy outcomes among South African women living with HIV.* AIDS, 2019. 33(5): p. 885-893.
4. Peltzer, K., V.J. Rodriguez, and D. Jones, *Prevalence of prenatal depression and associated factors among HIV-positive women in primary care in Mpumalanga province, South Africa.* SAHARA J : journal of Social Aspects of HIV/AIDS Research Alliance, 2016. 13(1): p. 60-67.
5. Hoffman, I.F., et al., *The Year-Long Effect of HIV-Positive Test Results on Pregnancy Intentions, Contraceptive Use, and Pregnancy Incidence Among Malawian Women.* JAIDS Journal of Acquired Immune Deficiency Syndromes, 2008. 47(4): p. 477-483.
6. Omani-Samani, R., et al., *Impact of Unintended Pregnancy on Maternal and Neonatal Outcomes.* J Obstet Gynaecol India, 2019. 69(2): p. 136-141.
7. Adeniyi, O.V., et al., *High rate of unplanned pregnancy in the context of integrated family planning and HIV care services in South Africa.* BMC Health Services Research, 2018. 18(1): p. 140.
8. Rucinski, K.B., et al., *Longitudinal patterns of unmet need for contraception among women living with HIV on antiretroviral therapy in South Africa.* PloS one, 2018. 13(12): p. e0209114-e0209114.
9. *Towards the Elimination of Mother-To-Child Transmission of HIV.* 2010, World Health Organization. p. 10-13.
10. Myer, L., et al., *Optimizing Antiretroviral Therapy (ART) for Maternal and Child Health (MCH): Rationale and Design of the MCH-ART Study.* Journal of acquired immune deficiency syndromes (1999), 2016. 72 Suppl 2(Suppl 2): p. S189-S196.
11. Barrett, G., S.C. Smith, and K. Wellings, *Conceptualisation, development, and evaluation of a measure of unplanned pregnancy.* Journal of Epidemiology and Community Health, 2004. 58(5): p. 426.

12. Myer, L., et al., *Impact of antiretroviral therapy on incidence of pregnancy among HIV-infected women in Sub-Saharan Africa: a cohort study.* PLoS medicine, 2010. 7(2): p. e1000229-e1000229.

13. Homsy, J., et al., *Reproductive Intentions and Outcomes among Women on Antiretroviral Therapy in Rural Uganda: A Prospective Cohort Study.* PLOS ONE, 2009. 4(1): p. e4149.

14. Taulo, F., et al., *Fertility Intentions of HIV-1 Infected and Uninfected Women in Malawi: A Longitudinal Study.* AIDS and Behavior, 2009. 13(1): p. 20-27.

15. Burgos-Soto, J., et al., *Incidence of pregnancy after antiretroviral therapy initiation and associated factors in 8 West African countries.* Journal of acquired immune deficiency syndromes (1999), 2014. 67(2): p. e45-e54.

16. Kosgei, R.J., et al., *Impact of integrated family planning and HIV care services on contraceptive use and pregnancy outcomes: a retrospective cohort study.* Journal of acquired immune deficiency syndromes (1999), 2011. 58(5): p. e121-e126.

17. Haider, T.L. and M. Sharma, *Barriers to Family Planning and Contraception Uptake in Sub-Saharan Africa: A Systematic Review.* International Quarterly of Community Health Education, 2013. 33(4): p. 403-413.

SECTION D: APPENDIX

A. Future Fertility Intentions and Contraceptive Use Questionnaire

MCH-ART: Family Planning/Pregnancy intentions Phase 3 6wks pp PID: 3 - __ __ __ __ - __ __
Xhosa-English Version 2.1.2, 29 Jan 2013

		Visit Date: __ __/__ __ __/__ __ __ __
Siza kubuza imibuzo malunga nendlela zocwangciso oza kuzisebenzisa ukugqibela kwethu ukuthetha nawe: *We are now going to ask you some questions about your use of family planning methods since we last spoke to you:*		
1.	Ukugqibela kwethu ukuthetha nawe, sewuqalile ukucwangcisa? *Since we last spoke to you, have you started using any family planning method?*	Hayi *No* = 0 → **Gqithela ku Q4**/*SKIP to Q4* Ewe *Yes* = 1
2.	Ukube ngoEwe, usebenzisa oluphi uhlobo? *If yes, what method are you using?* Rhangqa zonke ozisebenzileyo *Circle all that apply*	a. Ipilisi eziselwayo *Oral contraceptive pill* b. Isitofu se-2('noristerat NET-en') *2-month injectable ('noristerat NET-en')* c. Isitofu se-3 ('depo,petogen') *3-month injectable ('depo, petogen')* d. Isivalo –mlomo wesibeleko (IUD) *Intra-uterine device* e. Isivalo nzala sabantu ababhinqileyo *Female sterilization* f. Isivalo nzala sabantu besikhomo *Male sterilization* g. Idyasi kamkhwenyana *Male condom* h. Idyasi kamkhwenyana (yabantu ababhinqileyo) *Female condom* i. Olunye uhlobo,cacisa _____ *Other method, specify*
3.	Ulufumana phi ucwangciso lwakho? *Where do you receive your family planning method from?*	Gugulethu MOU = 1 Gugulethu CHC = 2 Ezinye/*Other* = 3
4.	Ukugqibela kwethu ukuthetha nawe, wabonisana neqabane lakho ngocwangciso tshapho okanye ukukhulelwa? *Since we last spoke to you have you discussed family planning or pregnancy with your partner?*	Hayi *No* = 0 Ewe *Yes* = 1
Siza kubuza ngenjongo zakho zokumitha kwilixa elizayo: *We are now going to ask about your future pregnancy intentions:*		
5.	Cinga ngendlela oziva ngayo ngoku. Yeyephi kwezintetha zilandelayo echaza bhetele ingcinga zakho ngokuba nomntwana kwixesha elizayo? *Think about how you feel right now. Which of the following statements best describes your own thinking about having a child in the future?*	Ndingafuna ukuba nomntwana kwithuba lenyanga ezi-12ezizayo = 1 *I may want to have a child in the next 12 months.* Ndingafuna ukuba nomntwana ngelinye ixesha ingezizo inyanga ezi-12 ezizayo = 2 *I may want to have a child sometime in the future but not in the next 12 months.* Ndigqibe ukuba andifuni ukuba nomntwana kwixesha elizayo = 3 *I have decided that I do not want to have a child in the future.* Andiqinisekanga ukuba ndiyamfuna okanye andimfuni umntwana kwixesha elizayo = 4 *I am unsure about whether or not I want to have a child in the future.* Okunye = 5,cacisa: _____ *Other = 5, specify*

Date completed: __ __/__ __ __/ __ __ __ __ Signed counsellor completing CRF: _____

Date of QC: __ __/__ __ __/ __ __ __ __ Signed measurement nurse: _____

Page **1** of **1** Initials of counsellor: _____

B. Ethical Approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room G50-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-enquiries@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

13 December 2019

HREC REF:792/2019

Dr K Brittain
Division of Epidemiology & Biostatistics
Office 5.47, Entrance 5
Falmouth Building-FHS

Dear Dr Brittain

PROJECT TITLE: EXAMINING THE ASSOCIATION BETWEEN FUTURE PREGNANCY INTENTIONS, CONTRACEPTIVE USE AND REPEAT PREGNANCIES AMONG WOMEN LIVING WITH HIV IN CAPE TOWN, SOUTH AFRICA. (SUB-STUDY - 451/2012) (MASTER'S DEGREE - MS L T MUBANGIZI)

Thank you for your response letter dated 06 December 2019, addressing the issues raised by the Faculty of Health Sciences Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 January 2021.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Ms Lilian Mubangizi will also be involved in this study.

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.

HREC 792/2019sa

Institutional Review Board (IRB) number: IRB00001938
NHREC-registration number: REC-210208-007

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use: Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines. The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

HREC 792/2019sa

C. MCH-ART ICAP IRB Approval

COLUMBIA|RESEARCH
Human Research Protection Office
Institutional Review Boards

June 6, 2019

Elaine Abrams
823100X - ICP ICAP

Protocol Number: IRB-AAAK8059
Title: Strategies to optimize antiretroviral therapy services for maternal & child health: the MCH-ART study
Grant #: 1R01HD074558-01
Approval Date: 06/04/2019 Expiration Date: 06/03/2020
Event Identifier: Renewal (Y08M00)

The above-referenced event was reviewed by Columbia University IRB 3.

Level of review and outcome: Approved by Expedited review

To view a list of documents that were included in this approval (if applicable) and all other currently approved documents for this study, please refer to the Print Menu for this Event in Rascal. It is important to confirm the status of each document, e.g., active, stamped, etc. Only stamped, active documents can be used with research participants.

Study Status: Closed to further enrollment: remaining research activities are limited to data analysis only

Modifications to the protocol included with this renewal:
- Changes in study personnel: removing Remien, Robert Howard;
- MCHART annual renewal 2018_approved

Please Note: Please address the following at the time of your next submission:
1. Exempt and Expedited page: please revise your answer to "No" for the question "Is the purpose of this submission to seek expedited review , as per the federal categories referenced in 45CFR46.110?"
2. Biological Specimens page: under the entry for blood, for the section "Description of Specimen and Method of Obtaining", please include the amount of blood to be collected and information related to how the specimens will be or have been obtained. For example, 15 ml of blood will be collected through a vein in the arm and an existing IV catheter, etc.

Important Reminder:
1. A request for continuation or completion of a research protocol is due at least 60 days before this research protocol's expiration date, unless otherwise requested by the Board. This renewal was submitted on 05/30/2019 with an expiration of 06/04/2019.
2. As this study is closed to enrollment, at the time of the next submission for this protocol (modification or renewal) please archive/detach ALL obsolete/older versions of documents not in use, including consent forms.

Electronically signed by: Collazo, Yaritza

154 Haven Avenue, 1st Floor New York, NY 10032 212-305-3883 Tel 212-305-1316 Fax
615 West 131st Street, 3rd Floor New York, NY 10027 212-851-7840 Tel 212-851-7044 Fax

Researcher Responsibilities:

Any proposed changes in the protocol must be immediately submitted to the IRB for review and approval prior to implementation, unless such a change is necessary to avoid immediate harm to the participants.

Any unanticipated problems that involve risks to subjects must be reported to the IRB in accordance with the Unanticipated Problems: Reporting to the IRB of Unanticipated Problems Involving Risks policy. All submissions for modifications and unanticipated problems must be submitted through Rascal.

Renewal applications should be submitted 60 days before the expiration date of this study through Rascal. Failure to obtain renewal of your study prior to the expiration date will require discontinuance of all research activities for this study, including enrollment of new subjects.

You must file a Closure Report in Rascal when your study has been completed.

D. MCH-ART UCT HREC Approval

UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences
Faculty of Health Sciences Human Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 6338 • **Facsimile** [021] 406 6411
e-mail: sumayah.ariefdien@uct.ac.za

24 October 2012

HREC REF: 451/2012

A/Prof L Myer
CIDER
School of Public Health & Family Medicine
FHS

Dear A/Prof Myer

PROJECT TITLE: STRATEGIES TO OPTIMIZE ANTIRETROVIRAL THERAPY SERVICES FOR MATERNAL & CHILD HEALTH: THE MCH-ART STUDY.

Thank you for addressing the issues raised by the Human Research Ethics Committee.

It is a pleasure to inform you that the Ethics Committee has **formally approved** the above-mentioned study including the following documentation:-

- Study protocol MCH-ART study: Version 1.2 (FINAL DRAFT, dated 08Oct2012)
- Phase 1 Informed Consent form: Version 2.0, 18 October 2012
- Phase 2 Informed Consent Form: Version 2.0 18 October 2012
- Phase 3 Informed Consent Form: Version 2.0 18 Oct 2012

Approval is granted for one year till the 28 October 2013.

Please submit a progress form, using the standardised Annual Report Form, if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC. REF in all your correspondence.

sAriefdien

Hrec/ref:451/2012 24/10/2012

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

This serves to confirm that the University of Cape Town Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.

The Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

sAriefdien

E. MCH-ART Informed consent forms

Phase 3 Informed Consent Form

TITLE OF RESEARCH: **Strategies to optimize antiretroviral therapy services for maternal & child health: the MCH-ART study**

WHAT IS THE PURPOSE OF THIS STUDY?
We are from the University of Cape Town and ICAP at Columbia University. You are being asked to take part in a study that is being conducted at the Gugulethu Midwife Obstetric Unit (MOU). The purpose of this study is to compare two different ways of providing HIV treatment to women after they deliver a baby.

We know that it is important for their own health as well as the health of their baby, that HIV-positive women receive the HIV care and treatment that they need both during and after delivery. Information learned in this study will help us to improve HIV services for pregnant women.

You are being asked to take part in this study because you are woman with known HIV infection who is currently breastfeeding a baby and who is taking HIV drugs. In addition, you have taken part in the previous phases of this study. The purpose of this consent form is to give you information to help you decide if you want to continue to take part in the last phase of this study.

WHAT DO I HAVE TO DO IF I AGREE TO TAKE PART?
If you agree to take part, you will be randomized (like a flip of a coin) to one of two places to receive your ART, as described below:

1. MCH-focused ART services group: Women assigned to this group will continue to receive HIV care and medicines here, at the MOU, as they did during their pregnancy. Their babies will also receive their routine baby care here at the MOU. When they have stopped breastfeeding, women in this group will be referred to their nearest general ART clinic, and their babies to their nearest City of Cape Town clinic for routine baby care

2. General ART services group: Women assigned to this group will be referred to the nearest ART clinic for HIV care and to continue their HIV medicines. Their babies will be referred to their nearest clinic for routine baby care.

   This is currently the standard of care for all HIV-positive women and their babies attending the MOU.

"Randomized" means that you will have a 50% chance of being in the group that will stay at the MOU to receive care. You will also have a 50% chance of being in the group that gets referred to an ART clinic. Neither the study staff nor you can choose which group you will be assigned to. The decisions are made by a computer and put into an envelope. The staff does not know which group is in each envelope.

This randomization will occur today and you and your baby will then come in for up to 6 additional study measurement visits at 6 weeks after delivery and 3, 6, 9, 12 **and 18 month**s after delivery. These study visits are separate from the usual clinic visits that you will have for your postpartum and HIV care. Study visits will be timed so that they take place on the same days that you come in for your usual postpartum and/or HIV care. Each visit will take about 30-60 minutes.

These visits will include the following:

- Answer questions about your recent pregnancy- and HIV-related health care, HIV disclosure, and use of HIV drugs (including side effects and adherence).
    - At selected visits, we will ask you additional questions about HIV, stigma, and mental health (including drug and alcohol use), family planning, infant feeding practices, infant health and health care and how you feel about the HIV care that you have received.
- Have 5mLs (1 teaspoon) of blood drawn from your arm
- Measurement of weight, length, head circumference and mid-upper arm circumference of your baby.
- Measurement of your height at the first visit and your weight and mid-upper arm circumference at all study visits

NOTE: The blood that is drawn at each visit will be stored and used to check your viral load (this is the amount of HIV in your blood) at a later time. Results from these tests will not be available to you, the clinic, or the study staff. When the health care providers at the clinic need to check your viral load, they will take a separate blood specimen. When it is stored, your blood and test results will not have your name or any other way of identifying you attached to it.

At both the 12 and 18 month visits, we will also draw blood from your baby:

- Baby will undergo a blood draw to collect up to 5ml of blood (no more than 1 teaspoon).
- This blood will be used to check your baby's HIV status.
    - We will return the results of this test to you as soon as it is available.

Follow-up of missed visits

You will be asked to provide contact information so that we may get in touch with you during the study. Study staff will talk with you about the best way to contact you. In the event that you miss one of the scheduled study visits, a member of the study staff will contact you in order to find another day and time to complete your visit. If you repeatedly miss study visits or the staff is unable to contact you using the information that you provide, it may be necessary to visit you at home in order to reschedule the missed study visit.

Contact for future study

After the completion of your last visit at **18 month**s **postpartum**, it is possible that we will contact you again at your next clinic visit or at another time in the future to take part in additional research studies. At that time, you would be asked to review and sign another consent form. You can choose to not take part in any future studies if you are asked. You will be asked to provide contact information so that we may get in touch with you regarding additional research studies. Study staff will talk with you about the best way to contact you.

WHAT ARE THE POTENTIAL RISKS?

You may feel uncomfortable about some of the personal questions you are asked. You may refuse to answer any question that you do not want to answer. There is some risk in sharing personal and medical information. We will be careful to keep all your information as private as possible.

Drawing blood is normally done as part of routine medical care and presents a slight risk of discomfort. Experienced staff will draw blood under sterile conditions in order to protect you against these risks.

WHAT ARE THE POTENTIAL BENEFITS?

There is no direct benefit to you if you take part in this study, but if we identify any health care problem for you or your baby during the course of the study, we will make sure you are referred to the appropriate health care services. In addition, the information gained in this study may help to improve ART services for HIV-infected pregnant women in Cape Town, the Western Cape Province, and across South Africa.

WHAT ARE THE ALTERNATIVES TO TAKING PART?

The alternative to taking part in this study is to continue with the standard of care for all HIV-positive pregnant women, which means you will be referred from the MOU to your nearest general ART clinic, and your baby will be referred to your nearest clinic for routine baby care, as soon as possible.

WHAT ABOUT CONFIDENTIALITY?

If you agree to take part, all information collected during the study will be kept strictly confidential. Your name will not be written on the study forms and will not be used in connection with any information or lab specimens that are collected as part of the study.

All study materials will be stored in locked filing cabinets. Only study staff and personnel involved in routine audits will have access to these materials. All staff involved in data collection and management will get specific training in confidentiality.

Even with these procedures in place, if the study staff learns that you are a risk to yourself or someone else or of possible child abuse and/or neglect, study staff will tell the proper authorities.

WHAT ABOUT INSURANCE?

There are no experimental medicines being used in this study. Therefore no insurance has been obtained. However you will be protected in terms of the study staffs' personal malpractice insurance or that of the university in the event of injury or illness that is caused by you taking part in this study.

If you sign this form, you do not give up any of the legal rights that you and your child have as research participants.

WILL I BE GIVEN ANYTHING FOR TAKING PART?

At the end of each visit, you will be given R20 in cash to cover the transport cost to your next scheduled study visit, and an R80 grocery voucher. Refreshments will be provided at all visits. You will also receive a small gift, up to the value of R50, at the final study visit when your baby is 12 months old.

ARE THERE ANY COSTS?

There is no cost for being in this study.

CAN I LEAVE THE STUDY?

You have the right to decide not to not take part in the study, to refuse to answer any questions, or to withdraw from the study at any time without any penalty. It will have no effect on the care that you receive at the Gugulethu MOU or any other health facility.

FUTURE USE OF SPECIMENS:

If you agree, any left over blood from the samples you have provided for this research project and the sample taken from your baby at the 12 and **18 month study visit**, may be used for future HIV and maternal and child health related research. It is possible that these stored samples may be tested to see if the HIV in your blood is resistant to any types of HIV medications or to look at other questions related to HIV. It is also possible that the stored blood from you and your baby may be used to look at other questions related to maternal and child health.

At this time, we cannot provide details of when this testing may be conducted. However, additional testing will not be done using these stored samples without the approval of the appropriate ethics committees involved in this research.

If you agree to let us keep your and/or your baby's stored samples for future research, they will be kept in a locked freezer for up to 5 years. If we do use the samples in the future, your name, your baby's name or other identifiers will not be included with this information (as with the rest of the information we collect for this study).

Please initial below to indicate whether or not you give permission for your and/or your baby's specimens to be used for future research. You may still remain in the study, no matter which you choose.

Consent for storage of your blood:

_____ (initial) I agree to have my blood stored for future research.

_____ (initial) I agree to have my blood stored for future research related to this study ONLY.

_____ (initial) I do **NOT** agree to the storage of my blood for future use.

Consent for storage of your baby's blood taken at the 12 and **18 month** visit:

_____ (initial) I agree to have my baby's blood stored for future research.

_____ (initial) I agree to have my baby's blood stored for future research related to this study ONLY.

_____ (initial) I do **NOT** agree to the storage of my baby's blood for future use.

DO YOU HAVE ANY QUESTIONS?
If there is anything that is unclear or if you need further information, please ask us and we will provide it.
Do you have any questions?

FOR ADDITIONAL INFORMATION:
If you have any questions or have any problems while taking part in this research study, you should contact:

Dr Landon Myer
School of Public Health and Family Medicine
Faculty of Health Sciences, University of Cape Town
Tel: 021 406 6661
Email: Landon.Myer@uct.ac.za

Dr Elaine Abrams
ICAP, Columbia University
Mailman School of Public Health
College of Physicians and Surgeons
Tel: +1 212 342 0543
Email: eja1@columbia.edu

If you have any questions about your rights as a research participant, you may contact the following member of the ethics committee:

Prof Marc Blockman
Chair, Human Research Ethics Committee
Faculty of Health Sciences, University of Cape Town
Tel: 021 406 6338

Columbia University Medical Center IRB
Tel: +1 212 305 5883

CONSENT STATEMENT:
I have read this form, or someone has read it to me. I have been offered a copy of this consent form. I was encouraged and given time to ask questions. I agree to be in this study. I know that after choosing to be in this study, I may withdraw at any time. My being in the study is voluntary. I understand that whether or not I participate will not affect my health care services received today, or at any time in the future.

Please indicate your consent with your signature.

Volunteer's name _____

_____
Signature of Volunteer Date

Staff member's name_____

_____
Signature of study staff Date

If the volunteer is unable to read or write the entire counselling process must be observed by an independent witness who can then confirm the procedure once the she has given consent.

Fingerprint of volunteer:

Witness:
I confirm that I am independent of the study and that I witnessed the entire informed consent counselling process in the home language of the volunteer
Name: _____

Signature: _____

Date: _____

Thank you.

F. JIAS author guidelines

Sections

1. Submission
2. Aims and Scope
3. Manuscript Categories and Requirements
4. Preparing the Submission
5. Editorial Policies and Ethical Considerations
6. Author Licensing
7. Publication Process After Acceptance
8. Post Publication
9. Editorial Office Contact Details

1. SUBMISSION

Please carefully read through the Instructions for Authors and prepare your manuscript according to the guidelines, including structuring it manuscript based on the chosen article category. Manuscripts that do not follow the instructions may be returned to the authors for corrections.

Authors should kindly note that submission implies that the content has not been published or submitted for publication elsewhere except as a brief abstract in the proceedings of a scientific meeting or symposium.

Once the submission materials have been prepared in accordance with the Author Guidelines, manuscripts should be submitted online at **https://mc.manuscriptcentral.com/jias**. *The submission system will prompt authors to use an ORCID iD (a unique author identifier) to help distinguish their work from that of other researchers.* **Click here** *to find out more.*

You will be asked to suggest potential peer reviewers for your manuscript: they should be experts in the field and be able to provide an objective assessment of the manuscript. Any suggested peer reviewers should not have published with any of the authors of the manuscript within the past five years, should not be current collaborators, and should not be members of the same institution. Suggested reviewers will be considered alongside potential reviewers identified by the Editorial team.

Click here for more details on how to use ScholarOne.

2. AIMS AND SCOPE

The *JIAS* welcomes submissions on HIV-related topics from across all scientific disciplines, including but not limited to:

- Basic and biomedical sciences
- Behavioural sciences
- Epidemiology
- Clinical sciences
- Health economics and health policy
- Operations research and implementation sciences
- Social sciences and humanities, including political sciences and media

The *JIAS* prioritizes submissions from operational research and implementation science as publication of such material can provide valuable information on various algorithms for monitoring and providing support for comprehensive, yet affordable and sustainable treatment, prevention and care programmes in different contexts.

Submission of HIV research carried out in low- and middle-income countries is strongly encouraged.

3. MANUSCRIPT CATEGORIES AND REQUIREMENTS

The *JIAS* accepts submissions in the following categories:

- **Research**
- **Short report**
- **Review**
- **Debate**

- **Commentary**
- **Letter to the Editor**
- **Viewpoint**

Research - full reports of data from original research studies

Abstract:
Headings: Introduction, Methods, Results, Conclusions
Word limit: 350 words

Main text:
Headings: Introduction, Methods, Results, Discussion, Conclusions
Word limit: 3500 words
Numbers of figures and tables: Unlimited
Additional files: Yes

Download the manuscript template

Short report - brief reports of data from original research, such as follow-up or confirmatory studies, case series and negative results

Abstract:
Headings: Introduction, Methods, Results and discussion, Conclusions
Word limit: 350 words

Main text:
Headings: Introduction, Methods, Results and discussion, Conclusions
Word limit: 2000 words
Numbers of figures and tables: 3
Additional files: No

Download the manuscript template

Review - comprehensive, authoritative descriptions and summaries of a specific subject area providing a systematic and substantial overview of the field

Abstract:
Headings: Introduction, Methods, Results and discussion (if applicable, otherwise Discussion only), Conclusions
Word limit: 350 words

Main text:
Headings: Introduction, Methods, Results and discussion (if applicable, otherwise Discussion only), Conclusions
Word limit: 5000 words
Numbers of figures and tables: Unlimited
Additional files: Yes

Download the manuscript template

Debate - presentation of an evidence-based argument

Abstract:
Headings: Introduction, Discussion, Conclusions
Word limit: 350 words

Main text:
Headings: Introduction, Discussion, Conclusions
Word limit: 3500 words
Numbers of figures and tables: 4
Additional files: No

Download the manuscript template

Commentary - focused and opinionated articles on important and timely issues, no original data

Abstract:
Headings: Introduction, Discussion, Conclusions
Word limit: 350 words

Main text:
Headings: Introduction, Discussion, Conclusions
Word limit: 2500 words
Numbers of figures and tables: 1
Additional files: No

Download the manuscript template

Letter to the Editor - comments on and responses to published articles

Abstract:
None

Main text:
Headings: None
Word limit: 500 words
Numbers of figures and tables: None
Additional files: No

Download the manuscript template

Viewpoint - constructive, stand-alone views on current topics

Abstract:
None

Main text:
Headings: None
Word limit: 1000 words
Numbers of figures and tables: 1
Additional files: No

Download the manuscript template

4. PREPARING THE SUBMISSION

Cover letter
In the cover letter, please explain why your manuscript should be published in the journal. If necessary, address any issues relating to our editorial policies .and declare any competing interests (see **Editorial Policies and Ethical Considerations**)

Parts of the Manuscript
The manuscript should be submitted as a main text file including figures and appendices and supporting information should be supplied as separate files.

Main Text File
The text file should be presented in the following order:

1. Title page;
2. Keywords;
3. Abstract;
4. Main text;
5. Conflict of Interest Statement;
6. Authorship;
7. Acknowledgments;
8. References;
9. Tables;
10. Figures;

Title page
The title should not contain abbreviations, except commonly used abbreviations such as HIV or AIDS (see **Wiley's best practice SEO tips**).

On the title page, you should mention the title of the manuscript, list all authors' names in full, and list any study groups if applicable. Each authors' affiliation should be numbered in superscript consecutively and listed underneath, including department, institution, city and country.

The corresponding author should be marked with the symbol § in superscript and full contact details should be provided, including a telephone number with country code. Authors who have contributed equally to the work should be marked with the symbol * in superscript. Deceased authors should be marked with the symbol ^ in superscript. The email addresses of all authors should be listed by their initials.

Keywords
Pease provide six keywords. Keywords should be taken from those recommended by the US National Library of Medicine's Medical Subject Headings (MeSH) browser list at **https://www.nlm.nih.gov/mesh/**. Preferably alternate words to those found in the abstract in order to improve search hits for the article in repositories.

Abstract
The Abstract should not exceed 350 words and should be structured according to the headings of the selected article category (see above), excluding the heading "Discussion" for Research articles. Avoid using abbreviations and do not cite references in the Abstract. If you are reporting results from a controlled health care intervention, please include your trial registry, together with your unique identifying number at the end of the Abstract. For randomized controlled trials, follow the **CONSORT extension for abstracts** .

Main Text

Article sections

Introduction
The Introduction section should introduce the topic to readers without specialist knowledge in that area and must clearly outline the current state of knowledge in this field, the motivation and the aim of the study or the article.

Methods
The Methods section should include all information necessary to repeat the study, in particular, the study design, how data was collected and analyzed, clarifying the choice of methods that were made. If applicable, you should describe the setting of the study, the dates the study were conducted, and the sample or participants, as well as necessary power calculations and materials, including statistical packages, used. Interventions and programmes should be described in detail. Generic names for drugs or any molecules should be used.

All studies involving humans or animals require a statement on ethical approval, and for the former, the consent procedure that was followed. Please include the names of the ethics review board(s) that approved the study. If the research study was specific to one sex/gender, the reasons for this should be clearly stated.

Results
This section should include only data and findings from the authors' study. Presentation of statistical results should mention confidence intervals and levels of significance where appropriate. Quotes from qualitative study participants of less than three lines should be quoted in the text using quotation marks. For quotes longer than three lines, place the quote in a separate, indented paragraph and introduce it with a colon. No quotation marks are needed in this case. Details of the participant can be added in round brackets following the quote, but should not contain identifiable information to ensure confidentiality. Clarifications within the quotation should be placed in square brackets.

Submitting authors are strongly encouraged to include data disaggregated by sex (and, whenever possible, by race) and provide a comprehensive analysis of gender and racial differences. The authors should include the number and percentage of men, women and, if appropriate, transgender persons who participated in the research study. Anatomical and physiological differences between men and women (height, weight, body fat-to-muscle ratios, cell counts, hormonal cycles, etc.), as well as social and cultural variables (socio-economic, education, access to care, etc.), should be taken into consideration in the presentation of data and/or analysis of the results.

Discussion
In the Discussion section, you should discuss your main findings and place these within the context of the current body of knowledge in the field. Limitations of the study, for example, selection bias, can also be discussed, and should address how these influence the results and conclusions. If statistically significant differences were found between men and women or between different racial or cultural groups in the effects of the studied intervention, the implications, if any, for clinical and/or public health should be adequately discussed.

Conclusions
In your Conclusions section, state your key messages from the study and explain their importance and relevance, as well as implications. Future studies and recommendations can be included in this section. The conclusions drawn must be strictly based on the data provided.

Conflict of Interest Statement
Authors will be asked to provide a conflict of interest statement during the submission process. For details on what to include in this section, see the 'Conflict of Interest' section in the **Editorial Policies and Ethical Considerations** section below. Submitting authors should ensure they liaise with all co-authors to confirm agreement with the final statement.

Authorship
Please refer to the journal's Authorship policy in the **Editorial Policies and Ethical Considerations** section for details on author listing eligibility. The individual contributions of each author must be specified in the Authors' Contributions section. Please use authors' initials and state that all authors have read and approved the final manuscript. An example of a suitable statement is: "S.W., N.J., D.W. and S.S. performed the research. S.W., N.J., H.H. and T.L. designed the research study. H.H. and S.S. contributed essential reagents or tools. S.W., N.J. and D.W. analysed the data. S.W. and N.J. wrote the paper." Please see the 'Authorship' section in the Editorial Policies and Ethical Considerations section below for what constitutes authorship.

Acknowledgments
Contributions from anyone who does not meet the criteria for authorship should be listed, with permission from the contributor, in an Acknowledgments section. Financial and material support should also be mentioned. Thanks to anonymous reviewers are not appropriate.

References
All external sources of information should be referenced within the text, the tables and figures, using consecutive numbering in square brackets, e.g. [1], [3-5], [3,4]. The references should be up to date and adequately reflect the current state of knowledge in the field. Citation bias, for example, by country or point of view must be avoided. Numbers of references are unlimited for all article categories and should be formatted in standard Vancouver style; **see Sample references from ICMJE** . Unpublished observations, personal communications and manuscripts currently under consideration should be cited in the text in round brackets and not in the reference list.

Tables
They should be supplied as editable files, not pasted as images. Tables should be inserted into the text. They should have the header: "Table 1. Title of table". All tables should be cited in the text in consecutive order. The tables should not contain colour or shading, and no vertical, visible lines. If tables are copied or adapted from another source, permission must be sought by the authors prior to publication and these should be clearly cited as such. If a table spans more than one page, authors may want to consider uploading the table as an additional file instead. Tables should be self-contained and complement, not duplicate, information contained in the text. A legend can be provided underneath the title, listing any abbreviations or meanings of symbols used. If several tables are included, please ensure that symbols are used consistently. Legends should be concise but comprehensive – the table, legend, and footnotes must be understandable without reference to the text. All abbreviations must be defined in footnotes. Footnote symbols: †, ‡, §, ¶, should be used (in that order) and *, **, *** should be reserved for P-values. Statistical measures such as SD or SEM should be identified in the headings.

Figures
Figures should be cropped as closely as possible and have the header: "Figure 1. Title of figure". All figures need to be cited in the text in consecutive order.

Although authors are encouraged to send the highest-quality figures possible, for peer-review purposes, a wide variety of formats, sizes, and resolutions are accepted. **Click here** for the basic figure requirements for figures submitted with manuscripts for initial peer review, as well as the more detailed post-acceptance figure requirements.

Figure legends should be concise but comprehensive – the figure and its legend must be understandable without reference to the text. Include definitions of any symbols used and define/explain all abbreviations and units of measurement. If several figures are included, please ensure that symbols are used consistently.

Additional Files

Appendices
Appendices will be published after the references. For submission, they should be supplied as separate files but referred to in the text.

Supporting Information
Supporting information is information that is not essential to the article, but provides greater depth and background. It is hosted online and appears without editing or typesetting. It may include tables, figures, videos, datasets, etc. **Click here** for Wiley's FAQs on supporting information.

Note : if data, scripts, or other artefacts used to generate the analyses presented in the paper are available via a publicly available data repository, authors should include a reference to the location of the material within their paper.

General Style Points
The following points provide general advice on formatting and style:

• *Abbreviations:* In general, terms should not be abbreviated unless they are used repeatedly and the abbreviation is helpful to the reader. Initially, use the word in full, followed by the abbreviation in parentheses. Thereafter use the abbreviation only.
• *Acronyms:* Acronyms should be used sparingly, and not in headings or in the Abstract. Only commonly known acronyms may be used, and they should be spelt out at first use followed by the abbreviation in brackets. SI units should be used, with litre and molar being permitted.
• *Units of measurement:* Measurements should be given in SI or SI-derived units. Visit the Bureau International des Poids et Mesures (BIPM) website **here** for more information about SI units.
• *Numbers:* Numbers under 10 are spelt out, except for: measurements with a unit (8mmol/l); age (6 weeks old), or lists with other numbers (11 dogs, 9 cats, 4 gerbils).
• *Trade Names:* Chemical substances should be referred to by the generic name only. Trade names should not be used. Drugs should be referred to by their generic names. If proprietary drugs have been used in the study, refer to these by their generic name, mentioning the proprietary name and the name and location of the manufacturer in parentheses.
• *Footnotes:* Footnotes are not allowed in the text, the information shall be included directly into the text, where it fits best, and if these are references, to include in the reference section at the end.
• *Language*: All submissions must be in UK English (International) and UN-accepted terminology should be followed. No capitalization should be used except for grammatically correct use, official names and titles, and abbreviations.
• *General recommendation:* Use line spacing of 1.5 and an easily readable font, for example, Times New Roman, size 12. Your manuscript should contain line numbers to facilitate editors' and reviewers' comments

Wiley Author Resources
Manuscript Preparation Tips: Wiley has a range of resources for authors preparing manuscripts for submission available **here** . In particular, authors may benefit from referring to Wiley's best practice tips on **Writing for Search Engine Optimization** .

Editing, Translation, and Formatting Support: **Wiley Editing Services** can greatly improve the chances of a manuscript being accepted. Offering expert help in English language editing, translation, manuscript formatting, and figure preparation, Wiley Editing Services ensures that the manuscript is ready for submission.

5. EDITORIAL POLICIES AND ETHICAL CONSIDERATIONS

Editorial Review and Acceptance
The acceptance criteria for all papers are the quality and originality of the research and its significance to journal readership. Except where otherwise stated, manuscripts are single-blind peer reviewed, meaning that reviewers remain anonymous to the authors, although the authors' identity is known to the reviewers. Papers will only be sent to review if the Editors-in-Chief determine that the paper meets the appropriate quality and relevance requirements.

All manuscripts are reviewed by at least two independent experts with experience in the subject area and selected by the Editors. Dedicated statistical reviewers may be used if needed. Reviewers have to declare any competing interests to the Editors. Authors can suggest peer reviewers during the submission step. Suggested peer reviewers should not have co-authored publications with any of the authors during the past five years, should not be current collaborators, and should not be members of the same institution. Suggested reviewers will be considered alongside potential reviewers identified by the Editorial team. Authors may also request exclusion of individuals as potential reviewers: those who have clear competing interests, are close collaborators, or have given input into the manuscript previously.

The Editors assess revised manuscripts based on whether the authors have adequately addressed all comments. Re-reviews are only requested when revisions fall out of the technical expertise of the Editors. Further rounds of major revisions are usually not allowed, and manuscripts that have not been satisfactorily revised will be rejected. Minor revisions though may be requested as needed.

Wiley's policy on the confidentiality of the review process is available **here**.

Data Storage and Documentation
The *Journal of the International AIDS Society* expects that data supporting the results in the paper will be archived in an appropriate public repository. Whenever possible the scripts and other artefacts used to generate the analyses presented in the paper should also be publicly archived. Exceptions may be granted at the discretion of the editor for sensitive information such as human subject data or the location of endangered species. Authors are expected to provide a data accessibility statement, including a link to the repository they have used, to accompany their paper.

Protein and nucleotide sequences
For nucleic acid sequences, protein sequences or atomic coordinates, which are cited in the manuscript, and the

accession number, together with the database where the information was deposited, should be cited in square brackets in the text, for example, [EMBL:AB026295, EMBL:AC137000, DDBJ:AE000812, GenBank:U49845, PDB:1BFM, Swiss-Prot:Q96KQ7, PIR:S66116]. Relevant databases are: EMBL Nucleotide Sequence Database (**EMBL**), DNA Data Bank of Japan (**DDBJ**), GenBank at the NCBI (GenBank), Protein Data Bank (**PDB**), Protein Information Resource (**PIR**) and the Swiss-Prot Protein Database (**Swiss-Prot**).

Mass spectrometry
Mass spectrometry data should be provided in the mzML format according to the **HUPO Protein Standards Initiative Mass Spectrometry Standards Working Group guidelines**. The data should also be deposited in the **ProteomeExchange** through the **PRIDE** website, and protein interaction data can be deposited through members of the IMEx consortium.

Structures
Protein structures can be submitted with one of the members of the **Worldwide Protein Data Bank**. Nucleic acid structures can be deposited with the **Nucleic Acid Database** at Rutgers. Crystal structures of organic compounds can be deposited with the **Cambridge Crystallographic Data Centre**.

Chemical structures and assays
Structures of chemical substances can be deposited with **PubChem Substance**. Bioactivity screens of chemical substances can be deposited with **PubChem BioAssay**.

Functional genomics data (such as microarray or CHIP-Seq data)
Please refer to standards proposed by the **Functional Genomics Data Society** and deposit your microarray data in MIAME-compliant format in one of the public repositories, for example, **ArrayExpress** or **Gene Expression Omnibus** (GEO). Deposition of high-throughput functional genomics sequencing data (such as RNA-Seq or ChIP-Seq data) with ArrayExpress or GEO in compliance with MINSEQE is also needed.

Computational modelling
Please prepare models of biochemical reaction networks using the **Systems Biology Markup Language** and submit your model to the **BioModels database**, as well as providing it as an additional file with your submission.

Plasmids
Please submit copies of your plasmids as DNA or bacterial stocks with **Addgene**, a non-profit repository, or **PlasmID**, the Plasmid Information Database at Harvard.

Ethical approval – Human and animal studies

Human Studies and Subjects
For manuscripts reporting medical studies that involve human participants, a statement identifying the ethics committee that approved the study and confirmation that the study conforms to recognized standards is required, for example: **Declaration of Helsinki**; **US Federal Policy for the Protection of Human Subjects**; or **European Medicines Agency Guidelines for Good Clinical Practice**.

A statement on the ethical aspects, including the consent procedure followed, must be included in the Methods section of the manuscript. The Editors may reject manuscripts where the research has not been carried out within an ethical framework. Images and information from individual participants will only be published where the authors have obtained the individual's free prior informed consent. Confidentiality of study participants must be ensured at all stages of research and reporting. Authors do not need to provide a copy of the consent form to the publisher; however, in signing the author license to publish, authors are required to confirm that consent has been obtained. Wiley has a **standard patient consent form available for use**.

Animal Studies
A statement indicating that the protocol and procedures employed were ethically reviewed and approved, as well as the name of the body giving approval, must be included in the Methods section of the manuscript. Authors are encouraged to adhere to animal research reporting standards, for example the **The Gold Standard Publication Checklist from Hooijmans and colleagues** or the **ARRIVE reporting guidelines** for reporting study design and statistical analysis; experimental procedures; experimental animals and housing and husbandry. Authors should also state whether experiments were performed in accordance with relevant institutional and national guidelines for the care and use of laboratory animals:

• US authors should cite compliance with the US National Research Council's **Guide for the Care and Use of Laboratory Animals**, the US Public Health Service's **Policy on Humane Care and Use of Laboratory Animals**, and **Guide for the Care and Use of Laboratory Animals**.
• UK authors should conform to UK legislation under the **Animals (Scientific Procedures) Act 1986 Amendment**

Regulations (SI 2012/3039).
• European authors outside the UK should conform to **Directive 2010/63/EU**.

Clinical Trial Registration
The journal requires that clinical trials are prospectively registered in a publicly accessible database and clinical trial registration numbers should be included in all papers that report their results. Authors are asked to include the name of the trial register and the clinical trial registration number at the end of the abstract. If the trial is not registered, or was registered retrospectively, the reasons for this should be explained.

Research Reporting Guidelines

Standard of reporting
The ***JIAS*** endorses international standards of reporting. Please see the **Uniform Requirements for Manuscripts Submitted to Biomedical Journals** guidelines produced by ICMJE as a reference standard of reporting. Authors are also referred to the **EQUATOR** network website for further information on the available reporting guidelines for health research, and the **MIBBI** Portal for prescriptive checklists for reporting biological and biomedical research where applicable. A number of checklists are available for various study designs, including randomized controlled trials (**CONSORT**), interventional trials (**SPIRIT**), qualitative research (**COREQ**), systematic reviews (**PRISMA**), observational studies (**STROBE**), economic evaluations of health interventions (**CHEERS**), meta-analyses of observational studies (**MOOSE**) and diagnostic / prognostic studies (**STARD** and **TRIPOD**). For systematic reviews, an additional file should be provided by the authors listing all details concerning the search strategy. Please refer to the **Cochrane Reviewers' Handbook** for an example of how a search strategy should be presented.

Guidelines on mutation nomenclature are provided by the **Human Genome Variation Society** , and authors should use the recommended gene name by referring to the appropriate genetic nomenclature database, for example, HUGO for human genes, and the International Committee on Standardized Genetic Nomenclature for Mice. When describing human phenotypes, please use standardized terms, such as those proposed by the Elements of Morphology working group (see **http://research.nhgri.nih.gov/morphology/index.cgi**).

Contributions from pharmaceutical companies or other commercial organizations should follow the **Good Publication Practice guidelinEs for pharmaceutical companies**, which also apply to any companies or individuals that work on industry-sponsored publications, such as freelance writers, contract research organizations and communications companies.

The ***JIAS*** supports international standards of reporting of trials, in particular, prospective registering and numbering of clinical trials. Clinical trials are defined by the World Health Organization as all phase I to IV trials, which are research studies that prospectively assign human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Trials need to be registered prior to submission in a suitable, publicly available registry. Links to existing registries can be found through ICMJE **here** or through the primary registers that participate in the **WHO International Clinical Trials Registry Platform.** The trial registration number should be included as the last line of the manuscript Abstract.

Reporting by gender and race
Submitting authors shall include data disaggregated by sex (and, whenever possible, by race) and provide an analysis of gender and racial differences. The authors should include the number and percentage of men, women and, if appropriate, transgender persons, who participated in the research study. Anatomical and physiological differences between men and women (height, weight, body fat-to-muscle ratios, cell counts, hormonal cycles, etc.), as well as social and cultural variables (socio-economic, education, access to care, etc.), should be taken into consideration in the presentation of data and/or analysis of the results. If statistically significant differences were found between men and women or between different racial or cultural groups in the effects of the studied intervention, the implications, if any, for clinical and/or public health should be adequately discussed. If the research study was specific to one sex/gender, the reasons for this should be clearly stated. Please refer to the **SAGER guidelines** for more information

Species Names
Upon its first use in the title, abstract, and text, the common name of a species should be followed by the scientific name (genus, species, and authority) in parentheses. For well-known species, however, scientific names may be omitted from article titles. If no common name exists in English, only the scientific name should be used.

Genetic Nomenclature
Sequence variants should be described in the text and tables using both DNA and protein designations whenever appropriate. Sequence variant nomenclature must follow the current HGVS guidelines; see **varnomen.hgvs.org**, where examples of acceptable nomenclature are provided.

Conflict of Interest
Authors are required to submit a statement on competing interests, which exist when personal or financial relationships with persons or organizations may influence the interpretation of the data or how the author's work is presented. For details, see ICMJE's policy on competing interests **here**. In brief, all financial competing interests must be disclosed in this statement (reimbursements, fees, funding, salary payments from or ownership of any stocks or shares in an organization that may in any way gain or lose financially from the publication of the manuscript, either now or in the future, or applications for patents relating to the content of the manuscript), as well as non-financial competing interests (such as political, personal, religious, ideological, academic and/or intellectual interests) that are related to the work submitted. The competing interest statement should be included in the manuscript and will be published in the final article. If no competing interests exist, please state in this section, "The authors declare that they have (or The author declares that he/she has) no competing interests."

Copyright and libel
Legal responsibility to ensure that no material is published that infringes copyright or that includes libellous or defamatory content lies with the Journal of the International AIDS Society's publisher, the International AIDS Society. If a manuscript is judged by the journal Editors to include potentially libellous content, authors will be requested to adjust wording as necessary.

Commercial writers and editors
The involvement of scientific (medical) writers or anyone else who assisted with the preparation of the manuscript content should be acknowledged, along with their source of funding, as described in the European Medical Writers Association (EMWA) **guidelines** on the role of medical writers in developing peer-reviewed publications.

Funding
Authors should list all funding sources in the Acknowledgments section. Authors are responsible for the accuracy of their funder designation. If in doubt, please check the Open Funder Registry for the correct nomenclature: **https://www.crossref.org/services/funder-registry/**

Authorship
It is understood that all authors listed on submitted manuscripts have read and agreed to its content, and meet the authorship requirements as detailed by ICMJE **here**. The list of authors should accurately illustrate who contributed to the work and how. All those listed as authors should qualify for authorship according to the following criteria:

1. Have made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data;
2. Have been involved in drafting the manuscript or revising it critically for important intellectual content;
3.Have given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content; and
4. Have agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. Acquisition of funding, collection of data, or general supervision of the research group, alone, does not justify authorship.

All contributors who do not meet the criteria for authorship should be listed in the Acknowledgements section. Examples of those who might be acknowledged include a person who provided purely technical help or writing assistance, or a head of department, who provided only general support. Prior to submitting the article all authors should agree on the order in which their names will be listed in the manuscript.

Additional Authorship Options: Joint first or senior authorship: In the case of joint first authorship, a footnote should be added to the author listing, e.g. 'X and Y should be considered joint first author' or 'X and Y should be considered joint senior author.'

ORCID
As part of the journal's commitment to supporting authors at every step of the publishing process, the journal requires the submitting author (only) to provide an ORCID iD when submitting a manuscript. This takes around 2 minutes to complete. **Find more information here**.

Publication Ethics
This journal is a member of the Committee on Publication Ethics (**COPE**) and endorses the World Association of Medical Editors' (WAME's) Policy Statement on Geopolitical Intrusion on Editorial Decisions. Note this journal uses iThenticate's CrossCheck software to detect instances of overlapping and similar text in submitted manuscripts. Any misconduct by authors in reporting their data, for example, falsification, will lead to rejection of their manuscript and other consequences decided on by the Editors. Please see COPE and International Committee of Medical Journal Editors (ICMJE) for further information on ethical issues in publishing

Read Wiley's Top 10 Publishing Ethics Tips for Authors **here**. Wiley's Publication Ethics Guidelines can be found **here** .

6. AUTHOR LICENSING

Journal of the International AIDS Society is an Open Access journal: authors of accepted papers pay an Article Publication Charge and their papers are published under a Creative Commons license. With Creative Commons licenses, the author retains copyright and the public is allowed to reuse the content. The author grants Wiley a license to publish the article and identify as the original publisher.

Open Access Fees: Information on the Article Publication Charge for publishing in the journal is available **here** .

If a paper is accepted for publication, the author identified as the formal corresponding author will receive an email prompting them to login to Author Services, where via the Wiley Author Licensing Service (WALS), they will be able to complete the license agreement on behalf of all authors on the paper.

To find out which Created Commons Licenses are available for the journal, click **here** . To learn more about Creative Commons Licenses and to preview terms and conditions of the agreements, please **click here**. Note that certain funders mandate a particular type of CC license be used; to check this, please click **here**.

7. PUBLICATION PROCESS AFTER ACCEPTANCE

Accepted Article Received in Production
When an accepted article is received by Wiley's production team, the corresponding author will receive an email asking them to login or register with **Wiley Author Services**. The author will be asked to sign a publication license at this point.

Proofs
Once the paper is typeset, the author will receive an email notification with the URL to download a PDF typeset page proof, as well as associated forms and full instructions on how to correct and return the file.

Please note that the author is responsible for all statements made in their work, including changes made during the editorial process – authors should check proofs carefully. Note that proofs should be returned within 48 hours from receipt of first proof.

8. POST PUBLICATION

Access and Sharing
When the article is published online:

• The author receives an email alert (if requested).
• The link to the published article can be shared through social media.

Promoting the Article
To find out how to best promote an article, click **here**.

Measuring the Impact of an Article
Wiley also helps authors measure the impact of their research through specialist partnerships with **Kudos** and **Altmetric**.

9. EDITORIAL OFFICE CONTACT DETAILS

Journal of the International AIDS Society
Avenue de France 23
CH - 1202 Geneva
Switzerland
Tel: 41 (0)22 7 100 800

Principal Contact
Editorial Team
Journal of the International AIDS Society
Avenue de France 23
CH - 1202 Geneva
Switzerland
Phone: 41 (0)22 7 100 800
Fax: 41 (0)22 7 100 899
Email: **editorial@jiasociety.org**